Neuroscience Research Australia Profile 2016

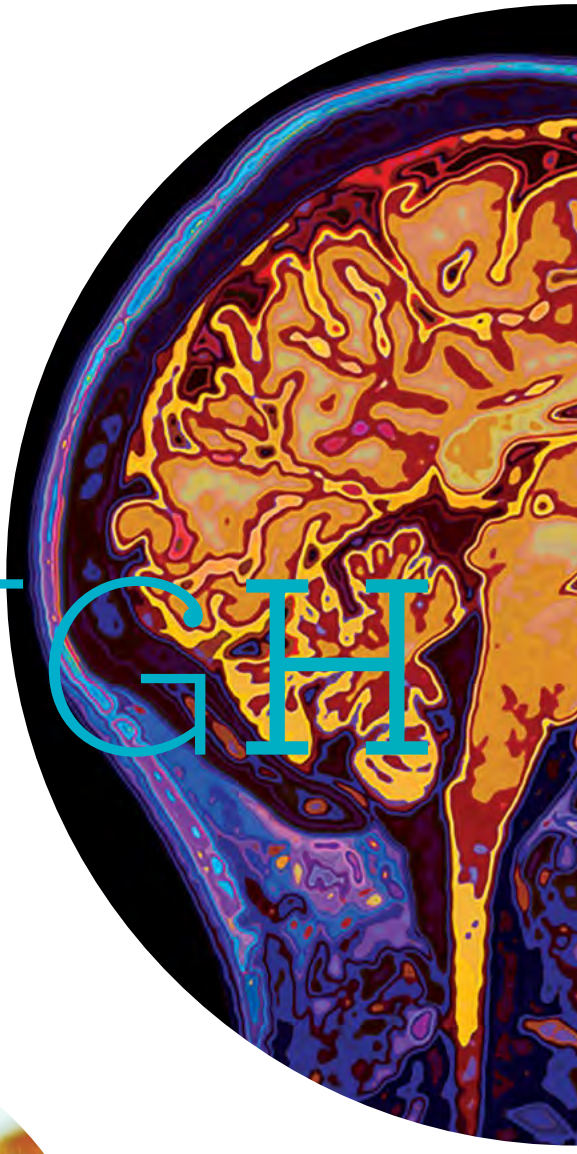
PROGR

Significant achievements in human progress have come from harnessing the power of medical research, technology and innovation to accelerate health interventions. At Neuroscience Research Australia, we continually seek new ways to deliver research outcomes capable of reaching more people and saving more lives. The potential for accelerating discovery has never been more tangible as we make significant progress in understanding factors underlying diseases and translating these into practical applications.

ESSION

"Our vision is to prevent and cure disease and disability of the brain and nervous system through leadership, excellence and innovation in neuroscience research."
This vision is reflected in the studies undertaken by our talented team of scientists and clinicians, touching the lives of all Australians, young and old. We have divided this Profile report into five sections: childhood, adolescence, adulthood, midlife and older age to reflect the considerable range and diversity of our research.

NeuRA
Discover. Conquer. Cure.



CHILDHOOD

Sense of self

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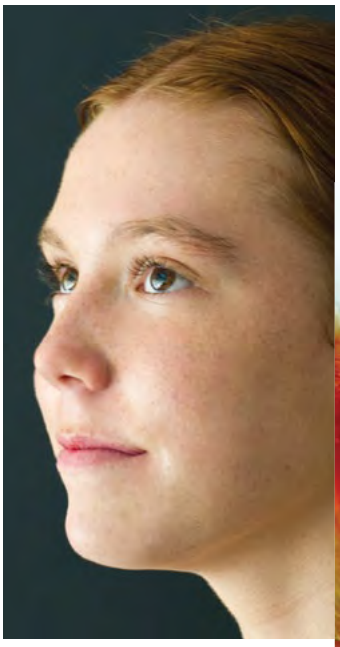
THROUGH



ADOLESCENCE

Teen mental health

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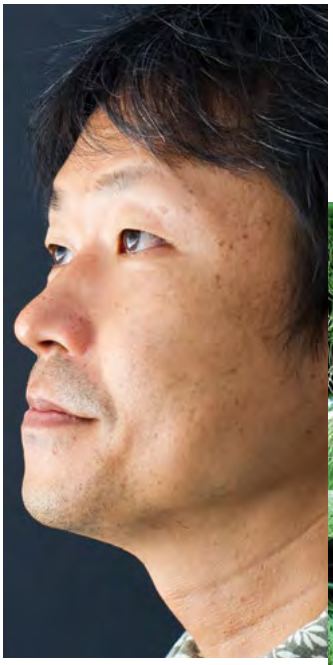

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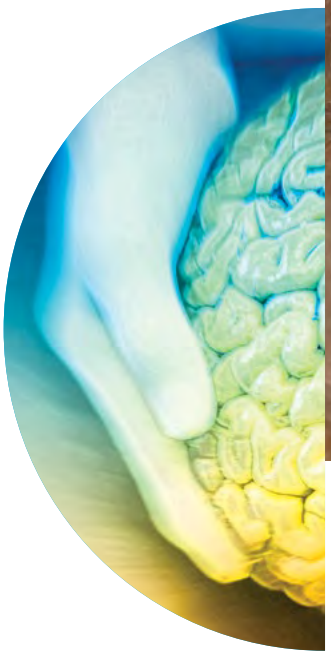

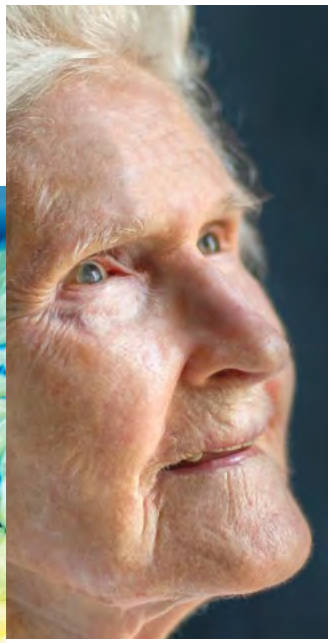

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The different dementias
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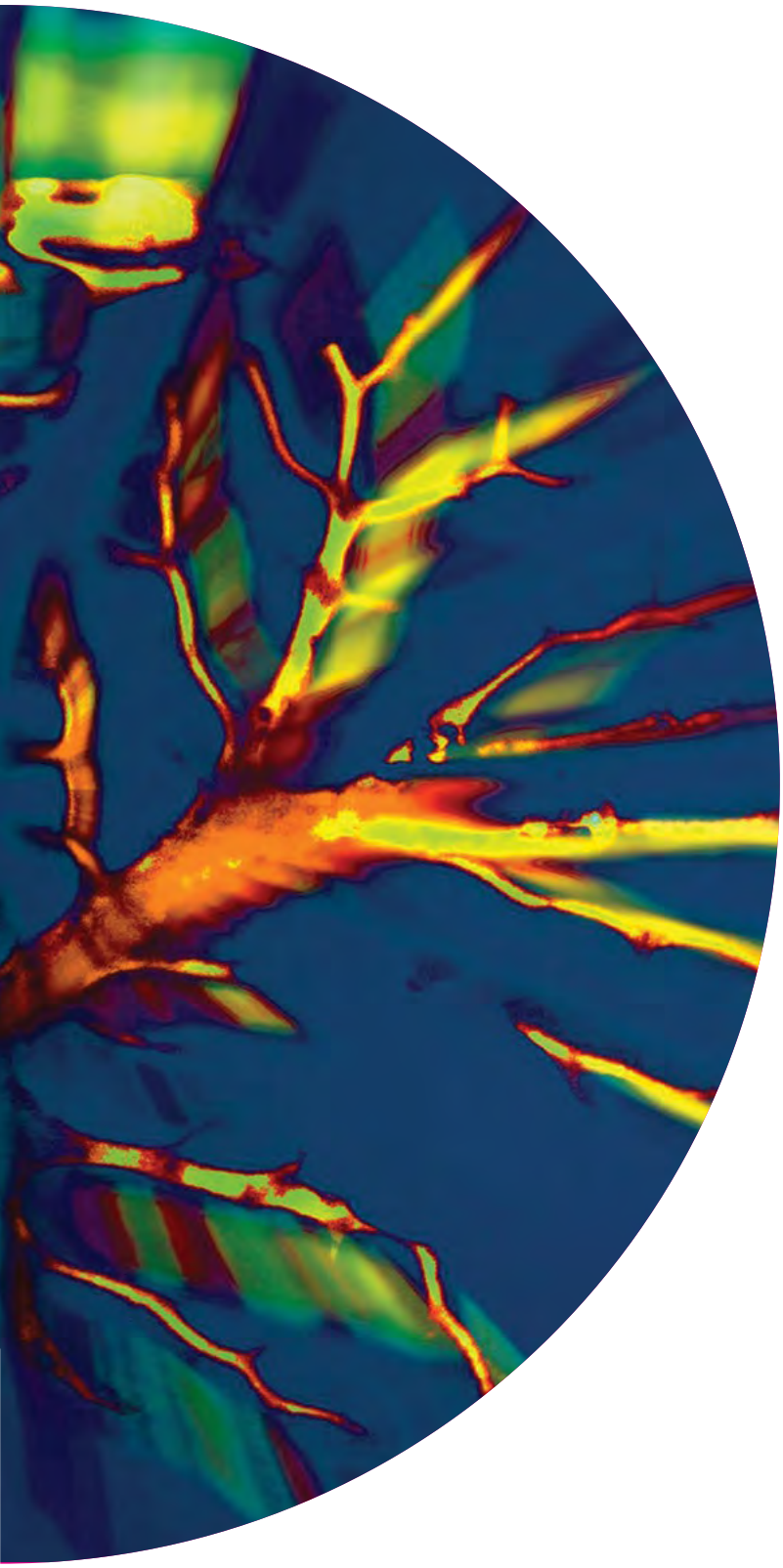
WELCOME

Progressive research is offering new hope across all ages



The most important investment in our country, from both a social and economic perspective, is in the wellbeing of its citizens through health and medical research. Tackling the growing impact of mental illness is imperative, and given our ageing population, the neurodegenerative conditions mean that over 350,000 Australians are living with dementia. This requires a sustained and comprehensive commitment from government, industry and philanthropy to underpin research to conquer and cure these disorders.

A $10 million grant from NSW Health, to match Margarete Ainsworth's generous donation, has been instrumental in funding the completion of the fitout of the Margarete Ainsworth Building. Level 6 now houses laboratories and offices for the Sydney Brain Bank and our dementia and Parkinson's research teams. New offices for our dementia clinical researchers are being constructed on Level 2 and the fitout of basement levels will provide a state-of-the-art gait laboratory for falls and movement studies, a new crash laboratory for injury prevention research, and dedicated storage for up to 2500 samples from the Sydney Brain Bank.

To combat the impact of illness, researchers worldwide must develop medical innovations based on sound scientific evidence. Clinical trials are key to improving the treatment of a particular disease or validating biomarkers to improve diagnosis. NeuRA has a number of clinical trials in place. Our participation in the international Dominantly Inherited Alzheimer Network (DIAN) prevention trial is groundbreaking because the identification of a successful drug has the potential to be effective in preventing Alzheimer's disease in later life.

NeuRA's merger with the Schizophrenia Research Institute has been a positive step for both organisations as we expedite translation of discoveries to benefit those living with schizophrenia. The Cognitive and Affective Symptoms in Schizophrenia Intervention (CASSI) trial verified that a drug that acts on estrogen hormone receptors in the brain reduces symptoms and improves cognition. Through the establishment of our Schizophrenia Research Council, we look forward to a stronger engagement with carers and consumers for input to enhance our research strategies.

In older age, falls are the leading cause of injury-related death and hospitalisation. NeuRA's Standing Tall study aims to improve balance and reduce fall risk via an exercise program delivered at home through an iPad.

NeuRA's achievements are a direct result of the dedication of our talented team of researchers, but the financial support we receive from government and our donors is essential.

We thank you sincerely.

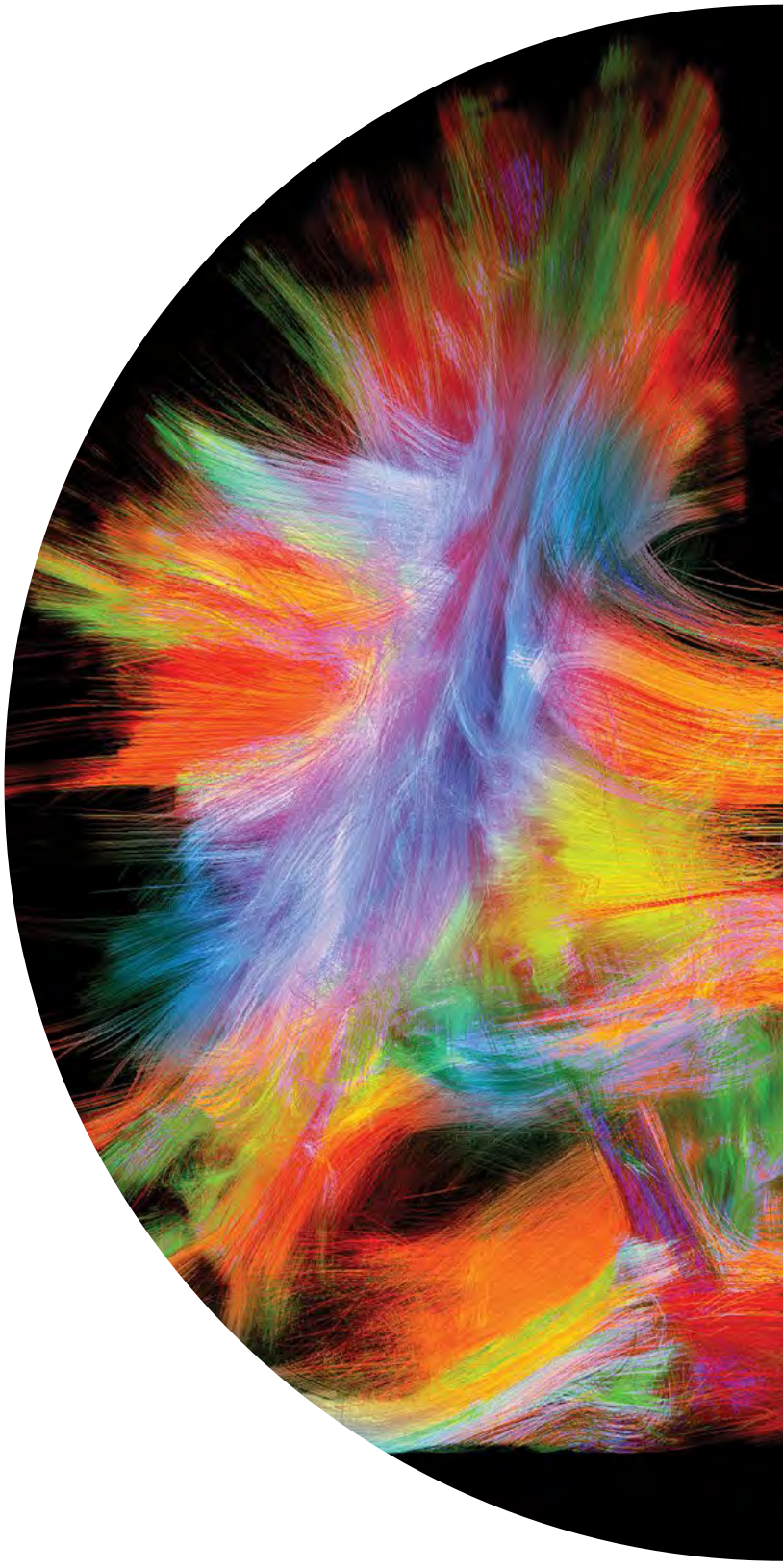
Paul V Brassil
CHAIRMAN

Prof Peter R Schofield
EXECUTIVE DIRECTOR & CEO

CHILDHOOD

SENSE OF SELF

Improving how children feel about themselves and others may have an important knock-on effect for their future mental health, especially if they experience psychotic-like symptoms.



Negative schemas, or self definition, are associated with psychotic-like experiences in children

In the first study of its kind, Dr Kristin Laurens has been part of a group of researchers interested in how schematic beliefs – that is, beliefs formed early in life and shaped by childhood experience – may be associated with unusual, or psychotic-like, experiences in children. It is thought that improving negative schematic beliefs in young people may be a useful therapeutic target for those at risk of developing psychosis.

Schemas influence how we interpret the actions of others, process our emotions and behave. If the schemas are negative they may cause a person to believe they are unlovable or worthless, or that other people are untrustworthy or judgemental. These negative beliefs about the self or others are more often seen in people with psychosis, when compared with the beliefs held by healthy individuals.

Psychotic-like experiences are non-clinical forms of symptoms that are reported by people with psychosis, such as hearing voices that others can't hear, feelings of being watched or having special power. These are common in young people in the general population, but persistence of these experiences is associated with distress and increases the likelihood of later mental health problems.

If addressed early, for example as part of a cognitive-behavioural intervention, the chance to improve negative schemas before they become fixed beliefs in adulthood may have beneficial outcomes for young people who have experienced distressing, psychotic-like experiences.

"Our study found that negative schemas in childhood are associated with psychotic-like experiences in children and that schema-change work is an important therapeutic focus," says Dr Laurens. "Such interventions include considering how the negative beliefs arose, how they are maintained, their influence on day-to-day functioning and the benefits of changing the incorrect beliefs."

An associated study has also found that these negative beliefs about self and others influence how the experience of being bullied impacts on children's psychotic-like experiences. "If we intervene early, we can teach these children ways to reduce their negative beliefs and build the kind of resilience that will help them better deal with victimisation experiences like bullying," says Dr Laurens. "Creating resilience is a great way to protect the future mental health of our children."

CHILDHOOD

Our early years are a crucial time for brain development, from the moment in utero when our neurons first begin to fire, to infancy when our neural networks make connections at a breathtaking pace. Our research at NeuRA starts at this critical phase of life.

CHILD RESTRAINTS

Seeking answers as to why injury still occurs during car crashes despite the high rate of child restraint usage.

Between 2002 and 2011 approximately 70 children per year were killed in car crashes, with approximately 3000 injured. This is despite the fact that close to 100 percent of Australian drivers with a child passenger use child restraints.

This alarming trend reveals that suboptimal child restraint use is a widespread problem that reduces crash protection and increases risk of injury. Dr Julie Brown and researcher Cameron Fong define suboptimal as the incorrect or inappropriate use of a restraint, the incorrect installation of a restraint or not putting a child in a restraint correctly. They also noted that this definition could include putting a child in a restraint that is not right for their size or age. For instance, putting a young child in a restraint meant for an older occupant. In an effort to understand why these mistakes may be occurring, the researchers explored whether or not parents' perception of their child's comfort played a role in the correct usage of restraints. Results have not confirmed this to be the case so far.

The study highlights the need for further investigation of the relationship between parent-perceived comfort and the actual comfort of the child, as well as the impact of child comfort on optimal child restraint use. "This is an important and complex issue to tackle," notes Fong, "and it's vital that we understand all of the possible issues surrounding incorrect restraint use in order to better protect our children."

Parents' perception of their child's comfort may play a role in the correct usage of restraints

Prof Lenroot is using magnetic resonance imaging in the autism spectrum disorder study

AUTISM

Understanding the difference between children with autism may help to predict their developmental outcomes.

Every person with autism is unique. But in order to understand what causes autism and develop treatments, researchers need to figure out what different people with autism might have in common as well.

"One approach is to look for subgroups of individuals within the umbrella of the autism spectrum disorders who may share specific neurobiological traits that might be related to clinical outcomes," says study leader, Prof Rhoshel Lenroot.

The research team is conducting a study in children with autism who are aged between 8 and 12 years.

"One of the differences that can be seen in children with autism is that some have gradually less severe symptoms as they become adolescents," she says. "Others may develop new problems such as worsening depression or irritability, and others stay the same."

The age range of 8 to 12 years is important because it is a time when factors related to pubertal development are starting to affect the brain. In this study, Prof Lenroot and team members are obtaining magnetic resonance imaging (MRI) and other measures of clinical and cognitive function, and then following the children for a year to see whether any factors at baseline may predict how they are doing a year later.

"Hopefully we will move towards better understanding and an appreciation of the diversity of people with autism, not only in research but also in their contributions to society as a whole," Prof Lenroot concluded.

CHILD MOTOR SAFETY

A new study is aimed at preventing serious injury.

Dr Chris Mulligan is calling for children who ride motorbikes, quads and other off-road vehicles to participate in a new study aimed at preventing crashes and serious injury.

The findings of a recent Queensland Coroner's inquiry into quad bike deaths highlighted the potential risks of children riding motorbikes and quads. There are more than 100 serious off-road crashes per year and the majority of those who are killed or seriously injured are children.

Unlike adults, children riding motorcycles and quads often don't have the physical strength or cognitive skills required to safely operate large vehicles.

"Childhood injuries and deaths from motorbike and off-road vehicle crashes affect children on farms and in rural settings far more frequently than children in metropolitan areas," says Dr Mulligan. "We know that these vehicles are often essential farming equipment, but we need to find out how they are being used in order to reduce the number of injuries."

Children don't have the physical strength or cognitive skills required to safely operate large vehicles such as quad bikes

"There have been a range of proposals aimed at reducing injuries such as changes to licensing or mandatory helmet use," he continues, "but we don't yet know what factors will work best, which is why this study is important."

By taking a quick survey, parents can help us identify the biggest risk factors for crashing and the areas where we can prevent the most injuries.

Dr Mulligan and colleagues from NeuRA are calling for the parents of children 16 years or under who ride motorbikes or off-road vehicles to take a short online survey asking about their riding behaviours, equipment and training.

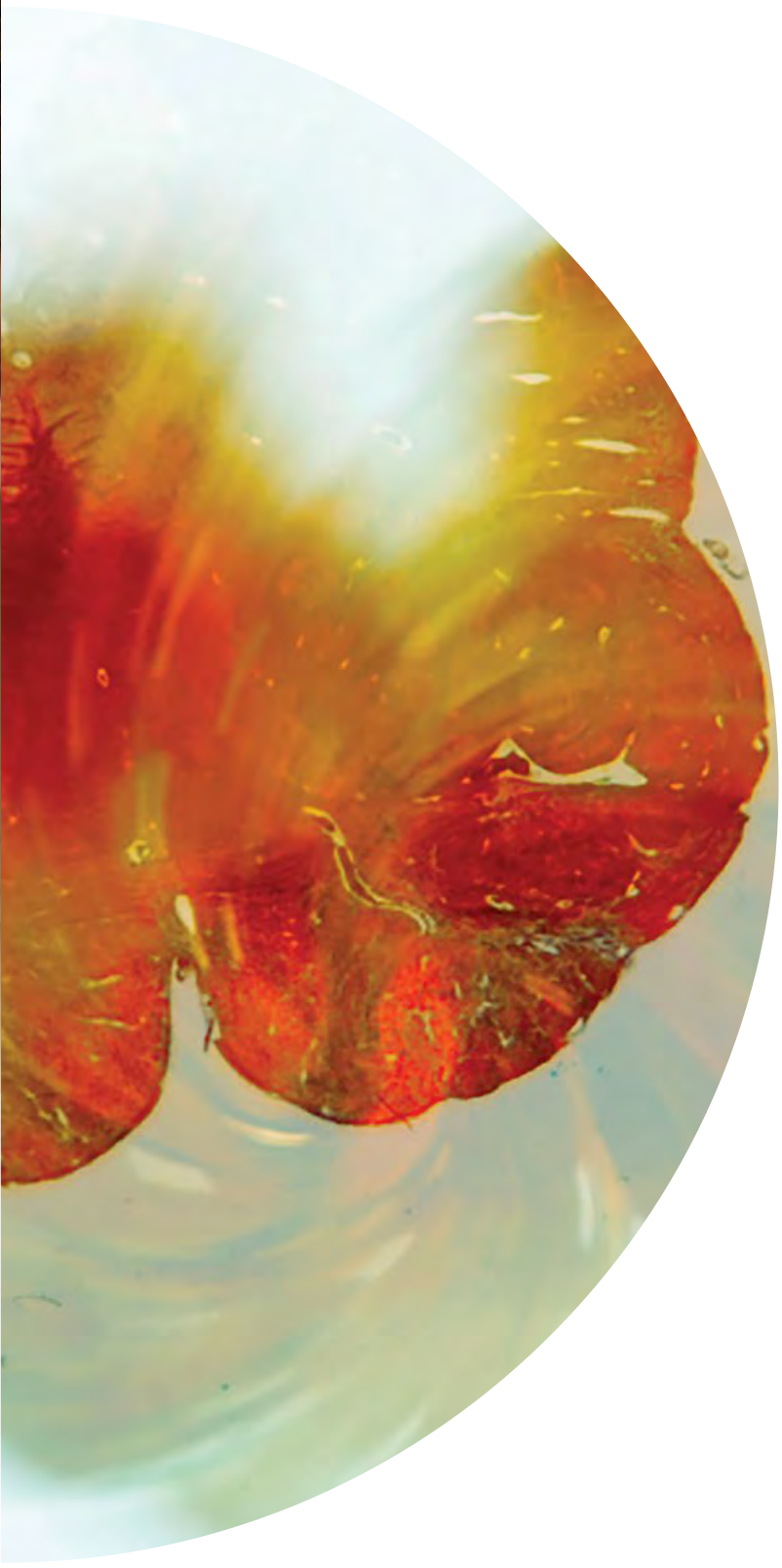
If you are interested in taking the survey go to: neura.edu.au/offroad

ADOLESCENCE

TEEN MENTAL HEALTH

Exposure to traumatic experiences in the early stages of life, including abuse or neglect, parental divorce or mental illness, and poverty, are known to influence the development of some mental illnesses.

Environmental influences can alter how our genes express themselves



These early experiences also have a great impact on a teen's developing hypothalamic-pituitary-adrenal (HPA) axis, which is the body's way of dealing with stress.

Prolonged exposure to these stresses has the potential to cause a variety of illnesses in adult life. Previous studies have noted that exposure to trauma in childhood can also affect cognition later in life for healthy adults, people with schizophrenia and people with borderline personality disorder. This caused our researchers to wonder if the gene, *FKBP5*, which is associated with an impaired stress response system, also had an effect on cognition in schizophrenia.

The study found that people who were exposed to childhood trauma and had a variant of the *FKBP5* gene, performed worse on attention tasks than did participants who were not exposed to childhood maltreatment.

The schizophrenia group, whether or not they experienced adverse situations as children, also shared a disease-associated marker that was associated with a worse performance on cognitive tests than the healthy controls.

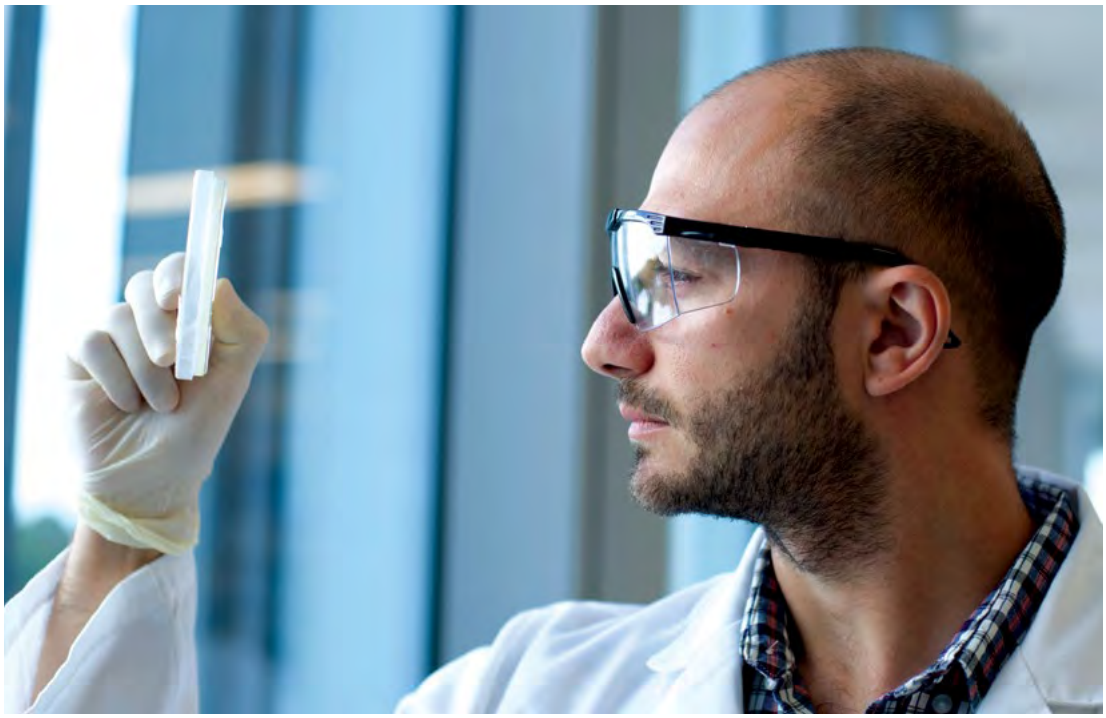
"This is a great example of how environmental influences can alter how our genes express themselves," says Assoc Prof Melissa Green. "The effect of poor childhood experiences on the *FKBP5* variant not only influences whether or not a mental illness may develop, but also seems to affect cognitive functions in healthy people. This is something we've not realised before now and opens the door to many new exciting research opportunities."

ADOLESCENCE

Adolescence is a critical time when the brain undergoes changes to prepare for adulthood. As the brain experiences a transformation, latent mental illnesses often first appear. On the cusp of maturity, teenagers face myriad challenges that can leave an indelible mark on the brain and nervous system.

BIPOLAR DISORDER

The discovery of genetic markers that determine how well a patient responds to lithium may change how bipolar disorder is treated.



A person's genetic make-up impacts how well they respond to lithium for bipolar disorder

Lithium is the most commonly prescribed mood stabilising drug used for the treatment for bipolar disorder. However it only works effectively in about a third of patients. Another third do partially well when prescribed lithium and the remaining third of patients do not respond at all.

Prof Peter Schofield and Dr Jan Fullerton at NeuRA and Prof Philip Mitchell at UNSW were contributors to the International Consortium on Lithium Genetics, which conducted a landmark study of more than 2500 people with bipolar disorder who had taken lithium.

The initiative examined the impacts a person's genetic make-up would have on the response to lithium. This research, published in the *Lancet*, has identified a region on chromosome 21 as being significantly associated with variation to lithium response, representing the first step in identifying the specific genes and molecular pathways underpinning response to lithium.

As the associated variants are quite rare, the clinical importance of these findings may be limited. However, the current shortage of good biomarkers of lithium response means that any robust genetic markers provide us with a real step forward.

The consortium plans to continue their work in better understanding the genetic signature that underpins lithium response by reaching out to other researchers around the world to increase sample numbers for an even more powerful study in the future.

SCHIZOPHRENIA

Themed issue of peer-reviewed journal *Schizophrenia Research* was guest-edited by Prof Cyndi Shannon Weickert.

Dr Tertia Purves-Tyson and PhD student Katie Allen worked with Prof Cyndi Shannon Weickert on a themed issue of *Schizophrenia Research*

> *"It's timely to consider the effect of sex hormones on schizophrenia given the recent success of our CASSI clinical trial."*

Prof Cyndi Shannon Weickert, with assistance from Dr Tertia Purves-Tyson and Katie Allen, was invited by *Schizophrenia Research* to bring together a collection of papers that examine the influence of hormones in schizophrenia.

"It was a real honour to be asked to do this," says Prof Shannon Weickert. "It's timely to consider the effect of sex hormones on schizophrenia given the recent success of our CASSI clinical trial. Because we had this breakthrough, we've gathered together recent studies that examine how sex hormones are involved and how we can better utilise them."

The articles in the special issue covered everything from basic research to clinical studies and offered insights into how hormones contribute to molecular and behavioural changes in schizophrenia. Although estrogens have received the most attention, it has become clear that testosterone and oxytocin may also play an important role in schizophrenia and the modulation of symptoms. Harnessing these hormones may lead to adjunctive therapies, especially targeting cognitive symptoms, which are currently the most disabling and untreated aspect of schizophrenia.

Themed issues of journals, which are often frequently cited, tend to garner more attention from their readership, which includes not just schizophrenia researchers but neuroscientists, psychiatrists and clinicians from around the world.

This special issue informed the schizophrenia research community of important studies which may guide the focus for future research.

LIKE FATHER LIKE SON

Childhood conduct problems are the greatest risk factor for antisocial behaviour and violence, as well as later adult mental health issues.

> *Some barriers may have to do with male gender roles, where dads assume that dealing with the children falls in the mother's domain.*

Research shows that parenting programs are more effective when fathers participate

Prof Rhoshel Lenroot is part of a large, multi-disciplinary team which seeks to improve the current treatments for children with conduct problems such as aggressive behaviours. One of the most effective ways to treat early conduct problems is through evidence-based parent training programs. Research has shown that participation reduces the early signs of violence and antisocial behaviour in children. The majority of participants in these programs are mothers, but there is evidence to show that children display greater improvements in behaviour when fathers participate in treatment, and that the benefits are maintained for a longer period of time.

The Like Father Like Son: A National Approach to Violence, Antisocial Behaviour and the Mental Health of Men and Boys project investigates innovative strategies for enhancing engagement of fathers in evidence-based interventions for childhood conduct problems at the national level. "Some barriers may have to do with male gender roles, where dads assume that dealing with the children falls in the mother's domain. Or there could be practical impediments," says Prof Lenroot.

The first step is a national survey of fathers to determine the barriers to involvement and design initiatives to overcome those. "Some initial research shows a much higher percentage of fathers participating if there are ways for them to do so." After-hours consultations and tailoring intervention programs will better appeal to fathers. The *Like Father Like Son* project will develop Australia's first free, national web-based parenting program to allow parents access to tips and strategies. The program will also design a training program for practitioners to equip them with skills to customise interventions to meet each family's unique needs.

If you are interested in further information about the project, go to: likefatherlikeson.com.au

CLINICAL TRIAL

> *The link between psychosis and inflammation of the brain is increasingly gaining attention worldwide.*

Clinical trial participant, Leanne O'Reilly, with Assoc Prof Tom Weickert and the CATS team

Assoc Prof Tom Weickert's clinical trial explores whether an anti-inflammatory treatment can reduce symptom severity and improve thinking ability in people with schizophrenia. His research may also have benefits for people with depression or bipolar disorder.

"The link between psychosis and inflammation of the brain is increasingly gaining attention worldwide," says Assoc Prof Weickert.

"It is being presented at many conferences and meetings, with whole sessions devoted to the topic. Whether inflammation causes psychosis or depression, or is a result of the illnesses is currently unknown; however there are currently effective ways to treat the inflammation."

The Canakinumab Add-on Treatment for Schizophrenia (CATS) study aims to identify people with schizophrenia who have the inflammation markers in their blood and assess if the treatment improves their thinking ability and reduces some of the symptoms associated with schizophrenia.

"Unlike current antipsychotic medications, which target fast-acting neurotransmitter molecules such as dopamine, this new treatment targets part of the immune system response (a cytokine receptor), which may be overactive in some people with schizophrenia and would cause damage to the brain," says Assoc Prof Weickert.

If successful, the CATS study may enable clinicians to perform specific biological assays, which includes testing for indicators of inflammation. This would mean that more appropriate, and thus beneficial, treatments would be available for some people who suffer from schizophrenia, schizoaffective disorder, bipolar disorder or depression.

If you are interested in participating in the study, phone 02 9399 1858.

BINGE DRINKING

Binge drinking – more than five drinks on one occasion – has become a common and more extreme pattern of drinking among young Australians.

A study underway at NeuRA assesses the effect of binge drinking on emotional processing as it has not been studied in adolescents previously.

Adolescence is a key period for teenagers to perfect their emotional skills that will enable them to function effectively as adults. Emotional behaviour, including detection of emotions in other persons, is based on the integrity of white matter fibres between key areas of the limbic system such as the amygdala and the prefrontal cortex.

"This study component was part of the Psychology Masters thesis of Emma Hubner," says Dr Lucette Cysique. "We assessed emotional facial recognition with the UNSW Faces task to measure recognition accuracy for sadness, anger, happiness, disgust and neutral emotion."

Left and right amygdala volumes were computed using gold standard manual tracing on each subject MRI. The study found that relative to abstainers, binge drinkers were less accurate at recognising angry faces. Binge drinkers and abstainers did not differ in the overall amygdala size. But the greatest ever number of drinks across all subjects was associated with smaller right amygdala volume.

In the binge drinking group, smaller right amygdala volume was associated with poorer processing of angry faces. Alcohol interference with home management and ability to work was associated with smaller right amygdala volume.

Overall, the study provides preliminary evidence of a relationship between adolescent binge drinking and emotion processing deficits, which particularly involve the integrity of the right amygdala and that contribute to measurable impact on social functioning.

Binge drinking in adolescence affects emotion processing

MODELLING SCHIZOPHRENIA

Genetic mouse models for schizophrenia: the candidate gene neuregulin 1.

Understanding mental and neurodegenerative disorders such as schizophrenia and Alzheimer's disease is the focus of Assoc Prof Tim Karl and his team. Behavioural phenotyping techniques and pharmacological tools are used to determine gene-environment interactions in the development of these illnesses. Another focus is the role of the endocannabinoid system in these disorders and the detrimental and sometimes therapeutic effects of cannabis plant constituents.

Schizophrenia is a chronic and disabling mental disorder that affects one percent of the world's population. Neither environment nor genetics alone is sufficient to cause schizophrenia. Rodent models for schizophrenia risk genes, such as the neuregulin 1 gene, are capable of partially modelling its aetiology and clarifying the impact of these genes on behaviour and brain development.

"To model schizophrenia in its full complexity," says Assoc Prof Karl, "it is important to develop multi-factorial animal models combining genetic and environmental schizophrenia risk factors, for example, cannabis abuse, diet and exercise. Our team focuses on the neuro-behavioural characterisation of these models, applying a multitude of different behavioural phenotyping paradigms."

Dr Justine Gatt is leading an international trial into youth resilience

RESILIENCE

> *Adolescents are particularly vulnerable to stressors as they are undergoing the final stages of development and are therefore highly susceptible to the impacts of their environment.*

The Youth Resilience Study is an international trial seeking ways to promote resilience across different cultural groups.

Promoting optimal mental health and resilience to trauma, adversity and stress is a prominent national and global priority. Resilience refers to the process of adaptive recovery from adversity; to maintain optimal levels of wellbeing such as life satisfaction, optimism, positivity and mastery in the face of dynamic challenges to psychological resources.

"With low resilience," says Dr Justine Gatt, "individuals are at high risk of developing psychiatric problems following adversity; depression and anxiety being the most common disorders. These disorders are defined by pronounced emotional and behavioural deficits to the individual which extend to marked alterations in brain structure and function.

Adolescents are particularly vulnerable to stressors as they are undergoing the final stages of development and are therefore highly susceptible to the impacts of their environment."

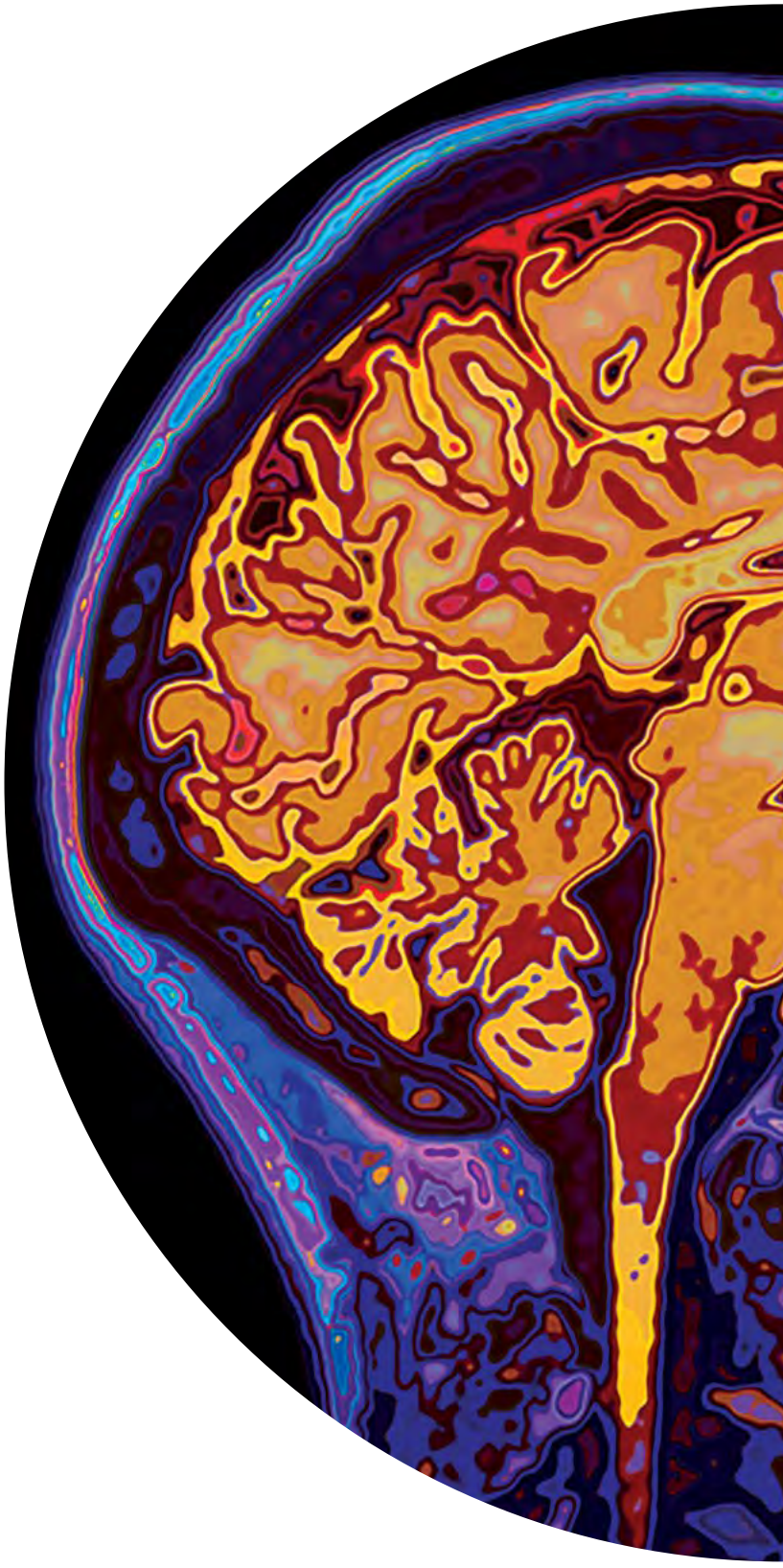
Dr Gatt is currently leading an international trial with other experts in resilience to understand youth resilience and ways to promote it across different cultural groups. The participating sites include Australia (Sydney), Canada, South Africa, UK, New Zealand and China. Each site is currently running a pilot study of questionnaires with approximately 30 to 50 participants in the 13 to 14 year old age group. The Sydney site will also conduct neurocognitive assessments in their participants. The information from this study will inform the role of various environmental, socio-ecological, neurocognitive and health factors that may contribute to resilience.

The findings will also inform the feasibility of running such a test battery in a larger, future two-year prospective trial across the sites. Importantly, the study will also identify key factors that should be promoted in national health policy to assist youth, to optimise their mental health and longevity, and to reduce healthcare costs for mental health and other related health problems.

ADULTHOOD

REAR SEAT SAFETY

There have been major advances in vehicle design that have led to significant reductions in death and injury to people in cars over the last few decades. But technologies introduced to keep rear seat passengers safe have not kept pace with technologies designed to keep front seat passengers safe.



Seat belts are incredibly effective in reducing risks in a car crash, so it is vital that those travelling in the back seat still buckle up

While road trauma has reduced considerably, it remains the leading cause of morbidity and mortality for people aged 15 to 44 years in developed nations.

Currently, there is a gap in understanding the sources and mechanisms of injury to rear seat occupants. In a recent study, NeuRA researcher Dr Julie Brown examined the pattern of injury and the causes that resulted in rear seat occupants sustaining injuries in frontal crashes.

She found that chest injuries were common across the age groups, and only those under the age of 15 also experienced head injuries. This was typically a result of colliding with the front seat. People aged between 16 and 50 most commonly received abdominal injuries and travellers over the age of 50 received fractures to the ribs or sternum. Seat belts were the common cause of the injuries.

“It’s important to remember that seat belts are incredibly effective in reducing the risk of death or injury in a car crash, so those travelling in the back seat of a car should still buckle up,” says Dr Brown.

The results of this study highlight the need to provide appropriate belt fit for the wide range of occupants who use the rear seat, and to control seat belt loads. Employing front seat technologies and novel technologies, such as inflatable seat belts to reduce head and chest injuries, would likely reduce the burden of injury among rear seat occupants.

“Possible improvements also include things like seat belt load limiters to help reduce rib fractures,” Dr Brown concludes.

ADULTHOOD

Adulthood is the prime of life for many, but it can also be a time when the unexpected occurs. Psychological or physical trauma can take many years to heal, and events related to poor cardiovascular health, such as stroke, can significantly affect the function of the brain.

MOTOR IMPAIRMENT

Motor impairment is a reduced ability to make well-controlled or forceful actions with the limbs.

Motor impairment is evident in a range of health conditions, including stroke, spinal cord injury, multiple sclerosis and frailty, with weakness an important aspect. Understanding how exercise training improves strength and performance may help researchers understand how the motor function of people with weakness can best be improved. When people start exercise training, the nervous system plays a big part in early strength gains. Changes in the motor areas of the brain contribute to improved strength, but the spinal cord is also likely to play a role. However, this has been difficult to show. Assoc Prof Janet Taylor and PhD student Jim Nuzzo set out to answer two questions: firstly, does the spinal cord become more excitable after one session of strength training, and secondly, does the type of strength training matter?

Able-bodied participants completed single sessions of different types of strength training using the upper-arm muscles. To assess spinal cord excitability, the team applied electrical pulses across the base of the skull to stimulate the corticospinal nerve fibres that carry signals from the brain to the motoneurones in the spinal cord. They measured the size of muscle responses evoked by this stimulation and found that excitability increased for 15 to 25 minutes after one session of strength training. This effect was observed with slow or fast contractions.

This result identifies the spinal cord as a site that undergoes early change with strength training. The increased excitability in the spinal cord after training implies that the muscles involved with training may become easier to activate. Such adaptations may be especially important for patients who are weak because of neurological conditions that impair muscle activation such as spinal cord injury or stroke.

MULTIPLE SCLEROSIS

A step-training video game designed for people with MS can improve not only balance but also thinking skills.

MS is an unpredictable, often disabling disease of the central nervous system that disrupts the flow of information within the brain, and between the brain and body. This results in muscle weakness, reduced motor coordination and execution, and impaired balance.

Falls are highly prevalent among people with MS. A study by Dr Phu Hoang and colleagues has shown promising results with a stepping exercise directly targeting critical balance issues that contribute to a person's risk of falling. This work now shows it is possible to modify key physical and cognitive risk factors for falls in people with MS.

Studies have shown that at least 50 percent of people with MS experience frequent falls. And of those who fall, 50 percent sustain injuries that require medical care. Fear of falling can cause people with MS to restrict their daily activities, with significant impacts on quality of life and general health. The study found improvements to reaction time and in upper limb dexterity. Together, these results suggest that the stepping exercise also improves the thinking skills needed to reduce the risk of falling. Based on these preliminary results, researchers will soon roll out a large-scale clinical trial to examine the full potential of this innovative program to reduce falls risk.

REHABILITATION

Correcting the 'scrambled' sensory map a stroke patient has of their hand may help to restore motor function.

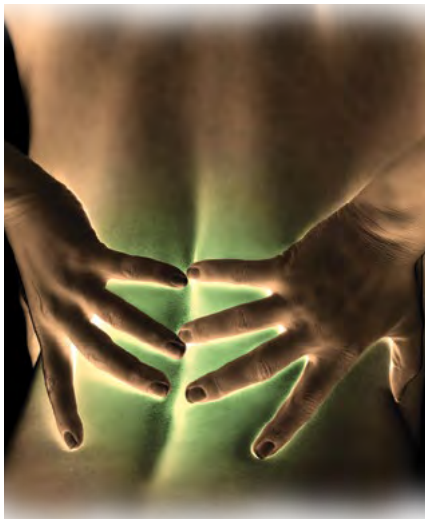
Dr Ingvars Birznieks: recovery of hand dexterity after stroke can be achieved

The hand is a powerful, sophisticated tool and sensory organ through which we interact with the world surrounding us. It is easy to comprehend consequences of lost hand function in amputees, but not so much for stroke patients whose hands seem physically intact.

The functionality of a hand relies on highly specialised fine-tuned communication between motor and sensory systems. Most rehabilitation strategies focus on motor function only; however, recovery of hand dexterity after stroke cannot be achieved in the absence of tactile sensation.

Very little is known about the nature of sensory disturbances and possible recovery of sensory function. Our research team has found that some stroke patients have a severely distorted or "scrambled" representation map of their hand. In these patients the brain has lost an orderly representation of the skin surface, so that when a patient is touched in one location on the hand, the sensation appears to originate from another site. This makes sensory information uninterpretable as it is like trying to describe an image from the pieces of a dis-assembled jigsaw puzzle. Besides obvious sensory consequences, this dysfunction may underlie poor recovery of motor function. Without appropriate sensory information it is impossible to regain skilled hand movements. This dysfunction has been shown to persist for many years after stroke, and may be more common than previously thought as it is generally not detected during routine neurological examination and patients themselves are not aware of it.

The most important question is: can we do something about it to facilitate rehabilitation and recovery? New evidence indicates that this is, indeed, possible. Those findings open doors for new rehabilitation strategies to be developed for chronic stroke patients. By delivering targeted rehabilitation, we hope to improve their chances to regain fine sensation and control over the affected hand.



CHRONIC BACK PAIN

Chronic back pain can change the way brains process information.

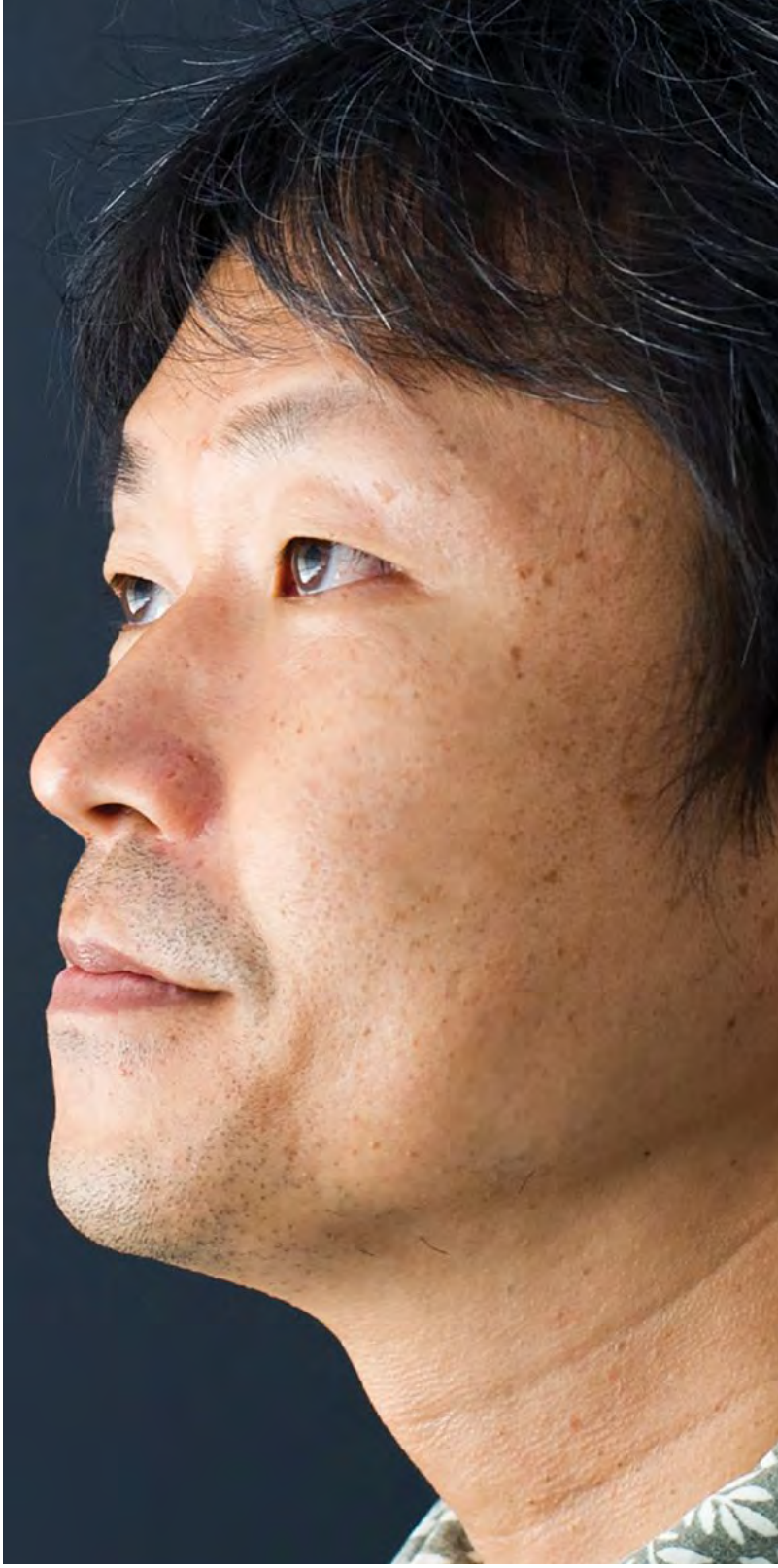
Chronic back pain researcher, Dr James McAuley, was involved in an international study that examined the relationship between chronic back pain and the volume of grey matter in particular areas of the brain. Chronic back pain is usually associated with significant disability and with changes to the individual's emotional state, most notably depression. This study compared the volume of grey matter in the brains of 111 people with chronic back pain to 432 healthy controls using a technique called voxel-based morphometry. This non-invasive neuroimaging technique allows researchers to investigate the structure of the brain.

The study found that people with chronic back pain had decreased volume of grey matter in areas of the brain associated with producing pain – for example, areas associated with the anticipation and unpleasantness of pain – as well as emotional regulation and with cognitive processing. "What this tells us is that the brains of people who have had back pain for a long time process everyday experiences differently from those who don't have pain. This could be contributing to the development and maintenance of back pain," says Dr McAuley. "We don't know what causes changes to the structure of the brain, but we hope to find this out in our ongoing studies so that we can open new avenues for treatment."

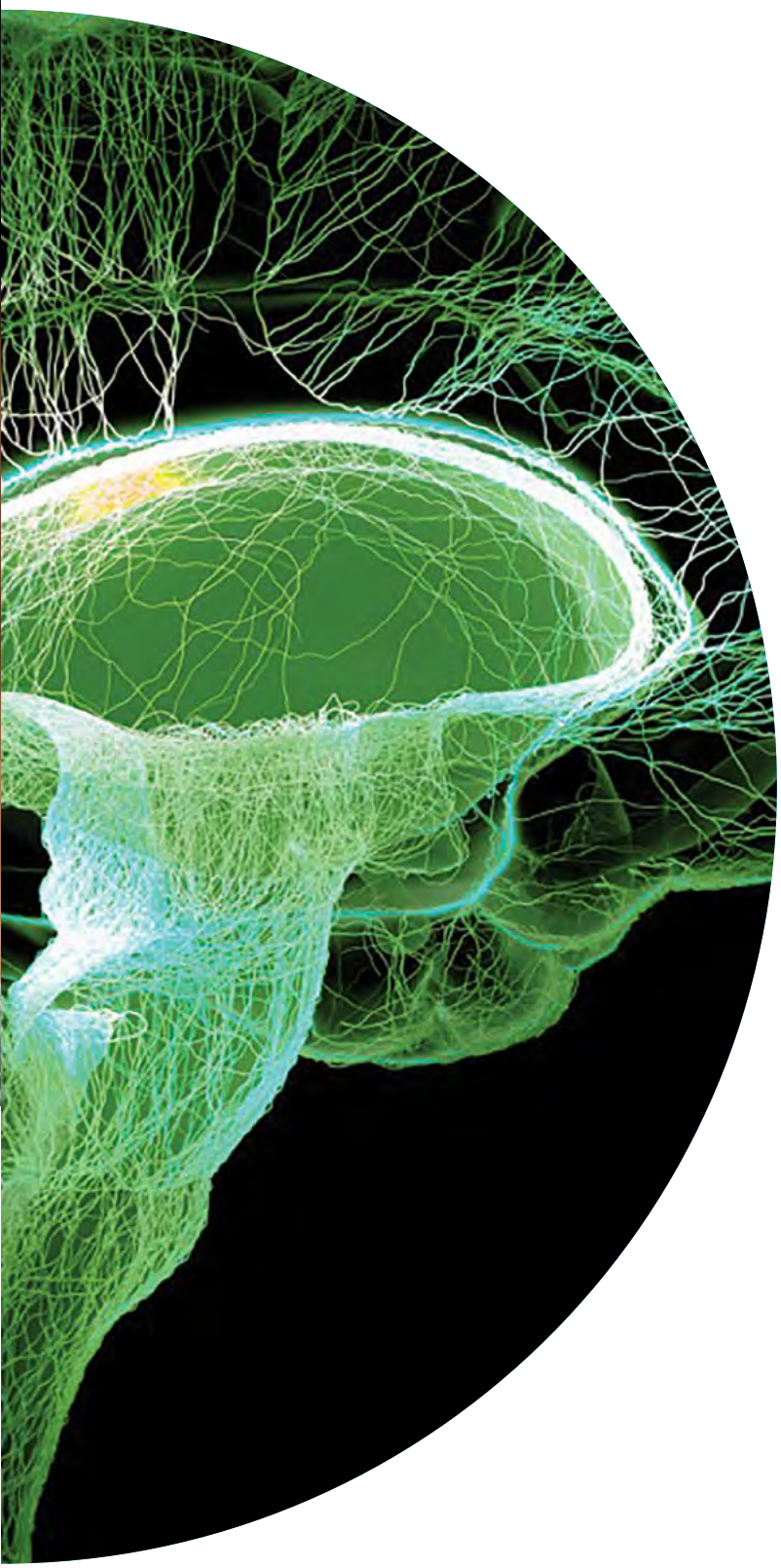
MIDLIFE

DIAN STUDY

An international landmark study continues to offer hope to families who are affected by early onset Alzheimer's disease.



The DIAN study aims to find a safe, effective medication for Alzheimer's disease



This rare, genetic form of Alzheimer's runs in families and typically affects people in midlife. Members of these families have been making a huge contribution to our understanding of the Alzheimer's disease process by participating in DIAN (Dominantly Inherited Alzheimer Network), an international study involving leading research groups in the USA, England, Australia, Europe, Asia and South America.

NeuRA has been involved in DIAN since 2009 with Prof Peter Schofield as Site Principal Investigator. By 2012, DIAN had clearly shown that the disease process in Alzheimer's disease begins at least 20 years before people develop symptoms of memory loss, and can be detected by special PET scans measuring brain amyloid deposition. This led to the establishment of prevention trials, in which drugs are given to at-risk family members to minimise the build-up of amyloid in the brain.

The first trial, DIAN-TU-001, is now fully enrolled, with 194 participants in 24 sites. The initial results are expected at the end of 2017, when everyone in the trial will have had two years of treatment with either an active drug or placebo.

Under the supervision of Dr Bill Brooks and Mirelle D'Mello, participants enrolled at NeuRA range in age from early 30s to early 50s. Most participants are working, raising families and leading busy lives, and we are very grateful that they are giving up their time for this quite demanding study. Every four weeks a nurse visits to give them either a 30-minute intravenous infusion or a subcutaneous injection of trial medication; once a year they come to NeuRA for several days of assessments and investigations, including an MRI scan, specialised PET scans and a lumbar puncture to collect spinal fluid.

The effectiveness of the study medications will be assessed initially by their influence on brain amyloid, as measured by special PET scans, and tau protein levels in the spinal fluid. If these show an effect, the trial will be extended for a further two years to see if there is an impact on memory function.

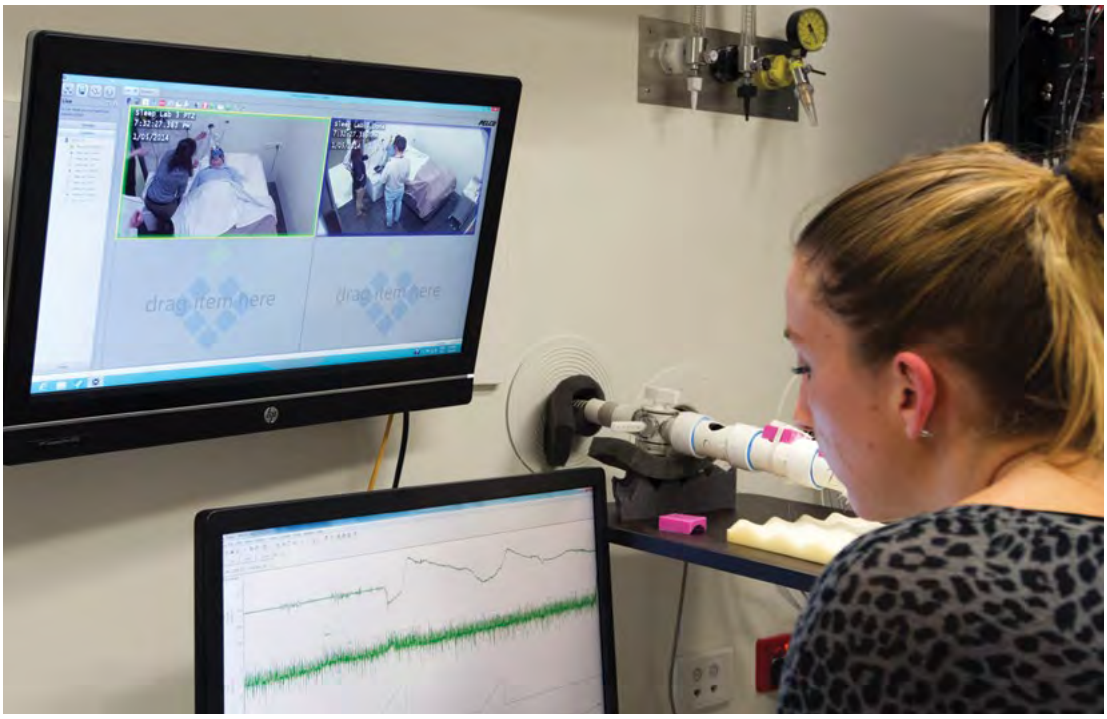
The DIAN Trials Unit aims to continue studying medications in this way until a safe and effective treatment is found. When a successful preventive drug is identified, it should also be effective in preventing Alzheimer's disease in later life.

MIDLIFE

Many baby boomers believe they will never have to slow down. Yet our research also shows that they are worried about their brain health. The 50s and 60s are when some types of dementias begin to appear, while something as seemingly innocuous as a sleep disorder can lay the foundations for poor health for the rest of their lives.

SLEEP APNOEA

Studies examine the effects of common sleeping pills on upper airway muscles and breathing during sleep.



The Sleep and Breathing Laboratory is investigating the use of sleeping pills in patients with OSA

Obstructive sleep apnoea (OSA) is a common sleep-related respiratory disorder and untreated OSA is associated with major adverse health and quality of life outcomes. Common sedatives may reduce OSA severity in some patients but worsen it in others. This is likely due to the underlying causes of OSA, which differ from person to person.

"A major concern regarding the use of sedatives in OSA is their potential to impair upper airway muscle activity which can worsen the condition," says Assoc Prof Danny Eckert.

"But a recent study by our sleep research team has shown that a common sleeping pill does not reduce upper airway muscle activity in people with OSA, as previously thought. This feature may certainly help some patients." Specifically, sleeping pills decrease a person's ability to wake up when their airway narrows. This can actually help some patients with OSA, such as those who wake up too easily, to achieve breathing stability by allowing them to get into deeper sleep. However, for people who don't wake easily these same pills can prolong breathing stoppages and worsen their oxygen levels.

A future study will focus on the physiological differences that may cause these diverse results in order to identify those who wake easily from sleep and for whom certain sedatives may be beneficial versus those who are harder to wake and for whom sedatives may be harmful.

> *"A major concern regarding the use of sedatives in OSA is their potential to impair upper airway muscle activity which can worsen the condition."*

FRONTOTEMPORAL DEMENTIA

A new screening test for dementia ensures that patients receive the most effective treatment sooner.

> *Any delay in starting early treatment significantly reduces the benefits, highlighting the importance of early and accurate diagnosis.*

A new, simple bedside screening test developed by Assoc Prof Olivier Piguet will help clinicians to determine whether a dementia patient has behavioural-variant frontotemporal dementia (bvFTD) or Alzheimer's disease (AD). In the frontal or behavioural variant of frontotemporal dementia, the person's mood and behaviour may become fixed and difficult to change, making individuals appear selfish and unfeeling. In contrast to Alzheimer's disease, recent memory is typically preserved.

Difficulty in reasoning, judgement, organisation and planning is frequent, along with a reduction in spontaneous conversation. Changes in eating patterns are also very common.

A decline in self-care and a reduction in the ability to perform activities of daily living is another early feature. As the disease progresses, the person may become 'obsessional', repeating patterns of movement and behaviours like handwringing or echoing back whatever is said.

BvFTD is often misdiagnosed as AD because the two dementias share clinical features; however they affect different brain regions and require alternative management approaches. The FRONTIER Executive Screen (FES) test will give medical professionals the confidence to make early, accurate diagnoses in around 10 minutes. "Rather than focusing on memory, the FES measures the integrity of complex thinking abilities," says Assoc Prof Piguet. "These functions are supported by the frontal lobes which undergo marked pathological changes in bvFTD, but are relatively spared in AD." In a study that compared the two groups, it was found that while both AD and bvFTD groups obtained lower FES scores compared to healthy controls, the bvFTD group was much more impaired than the AD group.

Knowing the type of dementia a patient has will inform their treatment management options. The few pharmacological dementia treatments currently available provide some cognitive and functional benefits to individuals with AD; however these same benefits do not extend to people with bvFTD. "Any delay in starting early treatment significantly reduces the benefits, highlighting the importance of early and accurate diagnosis," says Assoc Prof Piguet.

Assoc Prof Olivier Piguet: knowing the type of dementia a person has will inform their treatment options

EATING BEHAVIOURS

Dr Rebekah Ahmed: metabolic changes in MND and FTD might affect disease progression

Understanding what causes the changes in eating behaviours in people with frontotemporal dementia and motor neurone disease could potentially improve disease prognoses and progression.

Metabolic changes including fluctuations in weight, insulin resistance, and cholesterol levels have been identified in both motor neurone disease (MND) and frontotemporal dementia (FTD). Dr Rebekah Ahmed is exploring whether these metabolic changes are related and how they might affect disease progression — that is, whether they are caused by neurodegeneration or have a modulating effect on neurodegeneration.

FTD and MND are believed to represent a disease spectrum with overlap at both clinical and pathological levels. People with FTD often overeat, mistake inedible items for food or prefer sweet foods, while MND is generally associated with malnutrition. There are suggestions that nutritional intake might decrease as the disease progresses, particularly in patients with reduced functional capability.

The study found that the metabolic similarities in FTD and MND might represent additional components of the spectrum of these two diseases.

At one end of the continuum, patients with MND are likely to develop weight loss, hypermetabolism, malnutrition, hyperlipidaemia, and insulin resistance. At the other end, patients with FTD are likely to develop insulin resistance, and potentially less weight gain than would be expected in light of their increased caloric intake.

Further supporting the notion of the continuum between MND and FTD is evidence that patients with MND who develop additional cognitive deficits have an increased Body Mass Index compared with patients with MND without cognitive deficits.

Dr Ahmed is undertaking detailed assessment of both eating behaviour and metabolism in MND and FTD. This study should yield essential insights into the complex association between eating, metabolism, and neurodegeneration.

As many patients and carers ask about modifiable factors, such as diet and lifestyle, clarification of these areas will enable the provision of targeted and accurate clinical advice.

STROKE

Cutting-edge imaging technologies are being used to understand what causes muscle contracture after a stroke and how we can improve treatments.

Prof Rob Herbert and PhD student Arkiev D'Souza are investigating three dimensional changes that occur in skeletal muscle in stroke-related-contracture using MRI and Diffusion Tensor Imaging (DTI). DTI combined with tractography is an emerging technology that has only been applied to skeletal muscle in the past decade.

There have been limited studies assessing how well this technique reflects the tissue being analysed. The researchers are investigating the validity of such models and plan to use this technology. The mechanisms that cause contracture are poorly understood and intervention strategies to treat contracture have been ineffective. There is a need to improve current understanding of contracture so that it can be treated effectively. In anatomy, there is a dependent relationship between structure and function. Having a clear representation of the muscle structure can provide information about muscle function, or lack thereof. Imaging modalities such as ultrasound have limitations through providing only 2D images. DTI and tractography have the potential to provide 3D measurements of muscle architecture. This technique could be used to quantitatively identify the differences between healthy muscles and those with contracture. Such differences would contribute to our understanding the structural adaptations that take in contracture, and could potentially lead to improved intervention strategies.

Prof Rob Herbert and PhD student Arkiev D'Souza: improved understanding of muscle contracture will lead to effective treatments

In addition to investigating contracture from stroke, the team also hopes to launch their investigation into muscle contracture related to cerebral palsy.

IMPAIRED EMPATHY

Neuroimaging identifies areas of the brain affected in different dementias leading to a lack of empathy in one.

A sense of empathy is essential for social functioning as well as for prosocial behaviour, which is characterised by having a sense of concern for other people's feelings and welfare. Impaired capacity for empathy represents one of the core clinical features of the behavioral-variant of frontotemporal dementia (bvFTD) with an early loss of empathy considered a primary symptom of the disease.

People with bvFTD typically display emotional blunting, decreased social interest, loss of affection and warmth, diminished responsiveness to the feelings of others, and an inability to understand and infer the beliefs and perspectives of others. These striking deficits have a profound impact on the patient-caregiver relationship. In contrast, interpersonal functioning is held to remain relatively intact in Alzheimer's disease (AD), despite marked cognitive decline.

Cognitive empathy is the ability to understand another person's emotional state. Affective empathy is the ability to share and respond appropriately to another's emotions. A study by Dr Muireann Irish aimed to compare the capacity for cognitive versus affective empathy in bvFTD and AD. MRI scans were taken to understand what structural differences in the brain may cause these changes.

The study's findings support the well-established observation of marked social cognitive deficits in bvFTD that occur across cognitive and affective forms of empathy. These socioemotional deficits reflect the degeneration of medial prefrontal, frontoinsular, and lateral temporal regions, which appear crucial for successful social cognitive functioning.

These results offer important insights into the neurocognitive mechanisms that underlie socioemotional changes in bvFTD and may lead to understanding how caregivers may better deal with these changes.

MULTIPLE SYSTEM ATROPHY

Dr Scott Kim: MSA may be related to increased iron levels in the white matter of the brain

> *These genes hold great promise as biomarkers that may allow the early detection and confirmation of MSA.*

A new study provides insights into MSA molecular pathology and identifies several new candidate genes for future investigations.

Multiple system atrophy (MSA) is a sporadic and rapidly progressive neurodegenerative disorder. MSA can be clinically similar to Parkinson's disease (PD), and early cases are often misdiagnosed as PD because they share common biochemical and clinical characteristics.

In order to better understand what happens in the early stages of MSA, which is distinct from what happens in PD, researcher Dr Scott Kim examined gene changes in the white and grey matter of the brain. He looked specifically at the frontal gyrus region, which is only moderately affected by MSA, so that any changes that were seen in how genes were expressed could be assumed to be a result of the development of MSA.

"This is the first study that has analysed how genes are expressed in brains affected by MSA, and in particular how it is expressed in grey and white matter of the brain," says Dr Kim.

"Our study suggests that at the first stage of gene expression, MSA pathology may be related to increased iron levels in the white matter of the brain and may cause genetic disturbances that lead to MSA," he says.

The team also found that genes associated with MSA are expressed differently in the two different tissue types, and identified further genes that were worthy of future investigations.

"These genes hold great promise as biomarkers that may allow the early detection and confirmation of MSA."

HIV & BRAIN AGEING

HIV-related brain abnormalities and injury under investigation.

The HIV and brain ageing research, led by Dr Lucette Cysique, examines the causes of HIV-related brain injury in persons who are successfully treated with antiretroviral drugs and have reached at least 45 years of age.

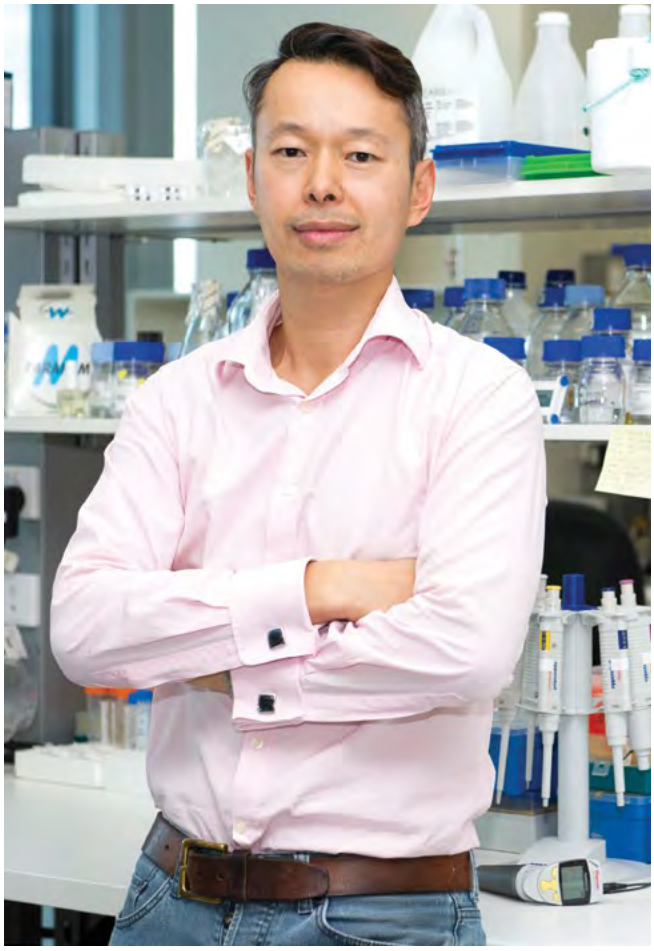
As part of the study, the participants underwent an MRI scan using a method called Diffusion Tensor Imaging (DTI). This method is designed to measure the brain's white matter integrity. The white matter is composed of bundles of myelinated axons, which connect brain regions.

HIV is known to alter white matter via inflammation, which then disrupts the connections between brain regions, especially between the deeper part of the brain and the frontal lobes. Ageing brain processes can also disrupt the same circuits. Therefore it is possible that ageing HIV+ persons may be at greater risks of white matter abnormalities.

A recent study by the group revealed a more complex picture. In the sample of patients that were successfully treated, the group detected evidence of brain repair marked by better white matter integrity as a function of historical immune recovery. In other words, the HIV+ persons who had the greatest recovery in their immune functions, once they started antiretroviral treatment, also had the strongest level of white matter integrity. This effect probably erased any combined HIV and age effect so much that there was no major white matter integrity difference between the HIV+ and age-comparable HIV-negative controls.

The group found that HIV disease duration and cardiovascular diseases, rather than age, were associated with a lower level of white matter integrity.

It will be important to follow-up this cohort as they reach their 60s and 70s.



Assoc Prof John Kwok: therapeutic possibilities of progesterone are promising

PROGESTERONE IN MND & FTD

The role of progesterone, identified as a potential therapy for MND, is being investigated for FTD.

Motor neurone disease (MND) is just one of the clinical syndromes associated with frontotemporal dementia or FTD. Others include corticobasal syndrome and progressive supranuclear palsy syndrome with a clinical variant of FTD being progressive non-fluent aphasia. FTD is difficult to diagnose because of the heterogeneity of symptoms, which can include cognitive, movement and language difficulties. Currently there are no approved medications indicated for treatment. The steroid hormone progesterone, which is thought to have neuroprotective functions in addition to its role in the female reproductive system, has been identified as a potential therapy for MND.

In line with this, high levels of endogenous progesterone have been shown to be associated with positive patient outcomes, and the hormone has also been used successfully to improve impaired motor phenotypes in a genetic mouse model of MND. The role of progesterone in FTD therapy has not been previously investigated.

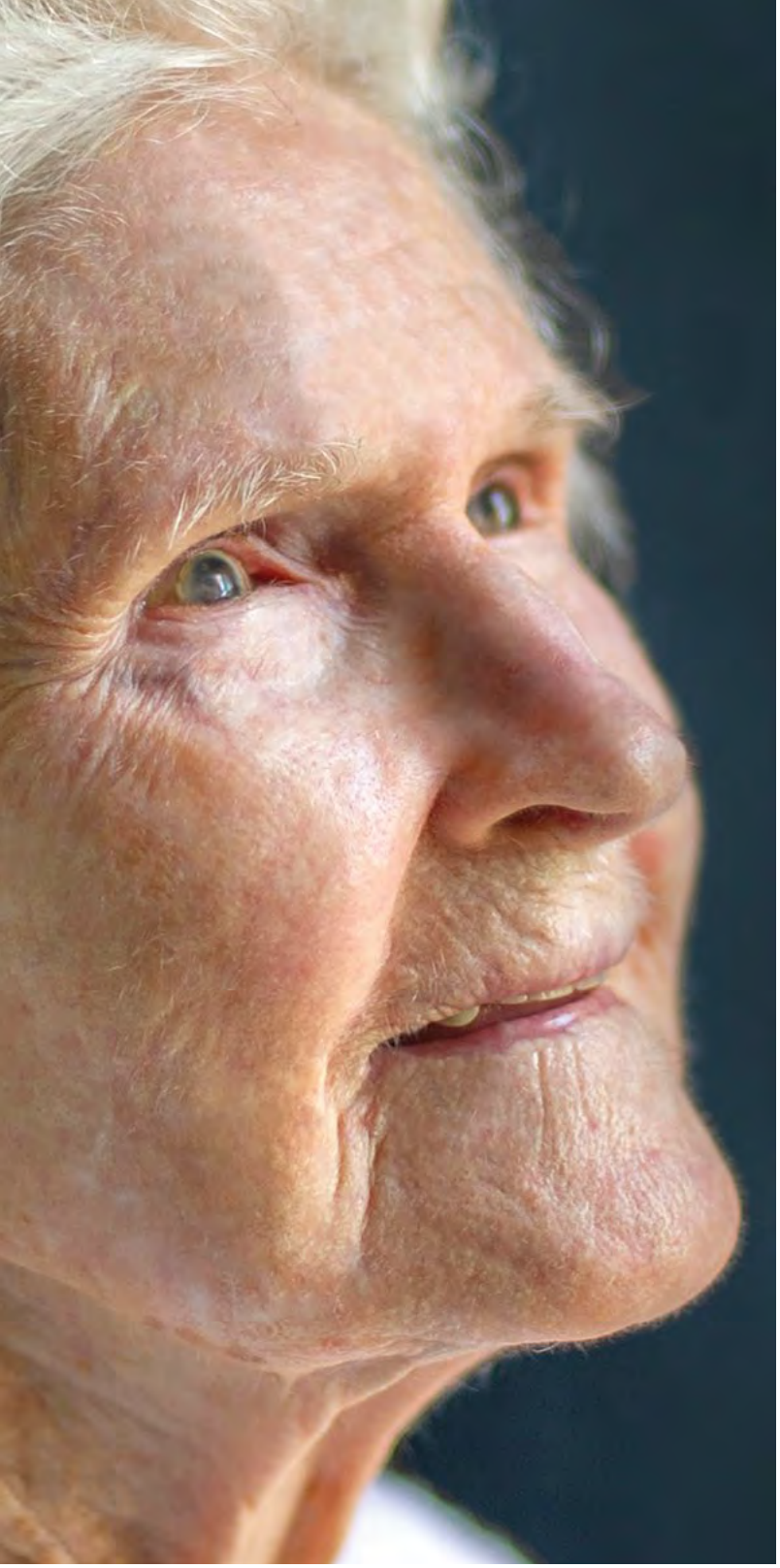
Assoc Prof John Kwok and team examined whether low levels of endogenous progesterone are associated with FTD, and whether exogenous progesterone can modulate the levels of the two major proteins associated with FTD pathology, namely Tau and TDP-43, in a cellular model. Finally, he examined the therapeutic efficacy of exogenous progesterone in a genetic mouse model of FTD.

Their results suggest that, as reported for MND, progesterone has an effect on disease parameters in FTD, suggesting that the effects of progesterone are mediated through changes in cellular Tau and TDP-43 protein levels. Progesterone also reduced disease severity in the genetic mouse model. Collectively, the clinical, cellular and animal data presented in their study suggest that progesterone might have therapeutic possibilities for certain clinical subgroups of FTD.

OLDER AGE

THE DIFFERENT DEMENTIAS

As part of the Federal Government's Boosting Dementia Research Initiative, NeuRA's Prof Glenda Halliday and the team she leads have been awarded one of six Dementia Research Team Grants. These five-year grants, will provide support for teams of researchers to pursue collaborative research, promote effective translation of research, and develop capacity under a dementia research priority framework.



Prof Halliday is looking specifically at the non-Alzheimer's disease dementias, such as frontotemporal dementia and dementia with Lewy bodies, which are often incorrectly diagnosed. "If you have a dementia syndrome, people are more likely to call it Alzheimer's disease," says Prof Halliday, who estimates that for every 1000 patients clinically diagnosed with Alzheimer's disease, just over half have the tissue pathology of Alzheimer's disease and about a third have a non-Alzheimer dementia. This is a figure that can only be arrived at via autopsy, so it is critical to find a way to accurately differentiate and diagnose the dementias earlier to ensure that the best treatment is provided.

"The interesting thing with Alzheimer's disease is that its progression is very slow and the majority of people will get it late in life," says Prof Halliday. "With non-Alzheimer's dementias, people get it earlier on in life and its progression is fast. So we really do need to develop a way to identify a dementia earlier for those people."

To achieve this goal, Prof Halliday will lead a collaborative group of ten teams from five different organisations as they study families with non-Alzheimer's disease dementias for the next five years to identify the genes involved, possible biomarkers to aid in diagnosis, and the different pathways each disease takes as it progresses.

"We're looking at families because researchers studying Alzheimer's disease have been able to identify early indicators so that we can treat people before the disease has an effect on the brain," says Prof Halliday. "We'd like to achieve the same outcome for other dementias. Certainly over the next five years we'll know more about what differentiates non-Alzheimer's dementias from Alzheimer's."

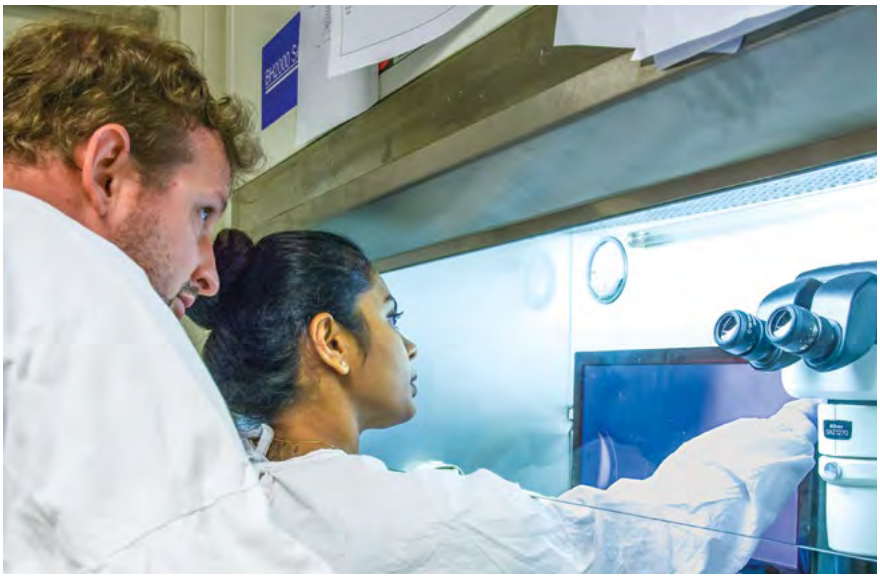
For every 1000 patients diagnosed with Alzheimer's disease, just over half actually have it

OLDER AGE

Growing old well is important to every one of us. We are investigating how we can maintain the health of the brain and body in older age by detecting dementias such as Alzheimer's disease, understanding the risks of having a fall in order to prevent them, and designing purpose-built technology to advance translational research.

PARKINSON'S DISEASE

A new study suggests that inflammatory profiles could be used to predict which people carrying a particular genetic mutation could go on to develop Parkinson's disease.



Dr Nicolas Dzamko and Research Assistant, Gayathri Perera: the team may have identified earlier biomarkers for PD

Parkinson's disease (PD) can be familial, meaning caused by genetic mutations passed through families, or it can be idiopathic, meaning the causes are unknown. Familial PD causes around 10 percent of diagnoses and often involves a mutation in the *LRRK2* gene, a variation of which has been linked to increased risk of idiopathic PD.

Dr Nicolas Dzamko and his team aim to determine if inflammatory markers are altered in healthy subjects carrying a *LRRK2* mutation (G2019S), and are genetically at risk of PD. They also aim to identify the differences in inflammatory markers between *LRRK2* G2019S-associated and idiopathic PD once the disease manifests.

"*LRRK2* is currently considered a compelling target for treatment," says Dr Dzamko. "There are drugs in advanced stages of development capable of blocking negative chemical alterations to the mutation. What is currently lacking is an understanding of why the mutation can result in PD. Results suggest that peripheral inflammation is higher in a percentage of subjects carrying the *LRRK2* G2019S mutation. These biological changes were observed prior to clinical symptoms that are currently used as the earliest indicators of PD."

The team's research may provide earlier biomarkers, or could identify *LRRK2* mutation carriers most at risk of conversion to PD. This could be important for deciding which patients might be enrolled in potential clinical trials of *LRRK2* drugs. When PD was manifest, those with the *LRRK2* gene did not differ from idiopathic PD patients, confirming previous studies suggesting that *LRRK2* associated PD is clinically similar to idiopathic PD. This could be important for helping to determine whether *LRRK2* blocking drugs might also work for idiopathic PD patients.

> *"Results suggest that peripheral inflammation is higher in a percentage of subjects carrying the LRRK2 G2019S mutation."*

SYDNEY BRAIN BANK

Dr Claire Shepherd and brain donor Marj Webb: the brain bank helps researchers better understand brain changes

> *If you're healthy and want to participate in NeuRA's studies and become a brain donor, this is the ideal program to assist with the continuation of our crucial research.*

Supporters over the age of 65 who want to take part in some of NeuRA's studies as healthy participants can also offer to join the brain donor program.

There's an essential need to understand how the brain changes during the ageing process and to understand the clinical consequence of these changes. To do this, the Sydney Brain Bank has created and is recruiting for the NeuRA Volunteers Brain Donor Program (NVBDP). This program recruits healthy individuals over the age of 65 from the NeuRA Research Volunteers Registry (RVR), which invites people to participate in a wide range of NeuRA studies, from falls and balance to MRIs.

When a volunteer passes away, the Sydney Brain Bank is able to look at changes that have occurred in the brain and investigate how that may have impacted on their performance in previous research, or whether such changes could be detected in their living scans. Researchers can then better understand the brain changes that underlie health and disease or dysfunction. Some of these studies will also provide crucial information regarding preclinical phases of some of the neurodegenerative disorders we study at NeuRA. Enrolling in the NVBDP is an incredible act of giving. Everyone who becomes involved has to first enrol in the RVR and indicate that they are willing to participate in any NeuRA studies. A participant must be healthy to do this. If enrolled and over the age of 65, you can participate in the NVBDP.

If you are healthy and want to participate in NeuRA's studies and become a brain donor, this is the ideal program to assist with the continuation of our crucial research.

If you are interested in further information, go to: neura.edu.au/sydneybrainbank

DEMENTIA & FALLS

> *We are currently assessing the program's ability to reduce the rates of falls in older people living in the community with cognitive impairment or dementia.*

A new program identifies and works with the preserved abilities and strengths of people with cognitive impairment to decrease their likelihood of falling.

Dementia is a neurodegenerative disease that affects memory, language, attention and problem solving abilities and affects between five and seven percent of people worldwide.

Falls are the leading cause of injury-related hospitalisation in people over 65 years of age and roughly a third of people aged 65 and over have at least one fall per year, which can result in pain, injury and loss of independence. People with memory problems or dementia have a much higher risk of falling. However, there have been very few studies that have investigated ways to prevent falls in this population. Prof Jacqueline Close and her team have developed an exercise and home hazard reduction program that is designed to work with the preserved abilities and strength of each participant. "We are currently assessing the program's ability to reduce the rates of falls in older people living in the community with cognitive impairment or dementia," says Prof Close. "We work with two groups – an intervention group and a control group."

Participants undergo an assessment at baseline followed by the same tests again at six and 12 months to compare how each of the groups performed on tasks involving strength and balance. What they're hoping to find is a reduced rate of falls during the 12-month study period. The intervention program involves both an exercise program and a home hazard reduction program that is delivered by experienced therapists and tailored to the participant's cognitive and physical abilities. Carers are an integral part of the intervention team, as some participants require supervision for exercise sessions. The NeuRA team works with carers to help them understand how to get the best from the person they are caring for, in terms of their functional cognition, completing the exercises and preventing falls.

Currently, there are no proven effective strategies for preventing falls in people with memory problems or dementia and this is the first study to potentially find a solution.

Jacki Wesson, Occupational Therapist with research participant, John: home hazard reduction programs are tailored to the participant's abilities

ABORIGINAL AGEING

Dementia prevalence is substantially higher in the majority of urban Aboriginal Australians.

Dr Kylie Radford: Ageing and Dementia in Aboriginal Australians project

Prof Tony Broe and Dr Kylie Radford have initiated the Ageing and Dementia in Aboriginal Australians project, which identifies causes of decline, promotes vitality and supports communities. Specifically, the project examines how to implement evidence-based healthy brain ageing (dementia prevention) programs in urban and regional Aboriginal communities.

It looks at dementia causes, prevention and care in Indigenous Australians, but will also be transferable to mainstream questions about the inter-relationships between head injury, stroke or vascular brain pathology, and amyloid deposition with Alzheimer's and vascular dementias – the common types of dementia found in all populations worldwide.

Dementia is a growing concern and burden on communities for Aboriginal Australians. This research will develop effective, culturally appropriate, and accessible strategies to promote healthy ageing and prevent dementia in Aboriginal communities. It will also investigate better ways to assess memory and thinking in this population, in order to identify changes as early as possible for enhanced dementia research and treatment prospects.

STANDING TALL

Dr Kim Delbaere and her research team have created a home-based training program app that can be loaded onto an iPad to help improve the balance of those over the age of 70, reducing their risk of falls.

We know that balance training can prevent falls in older people; however long-term participation in these types of exercise programs can be poor due to the boring nature of repetitive exercises.

Dr Kim Delbaere's falls and balance team at NeuRA, has recently focussed on finding solutions to help older people do the necessary exercises for them to stay independent.

This work has led to the development of new technology-based solutions such as the Standing Tall home-based exercise program using an iPad app. By using this technology, the team hopes to provide a more convenient way for informing and guiding people towards effective exercises for preventing falls.

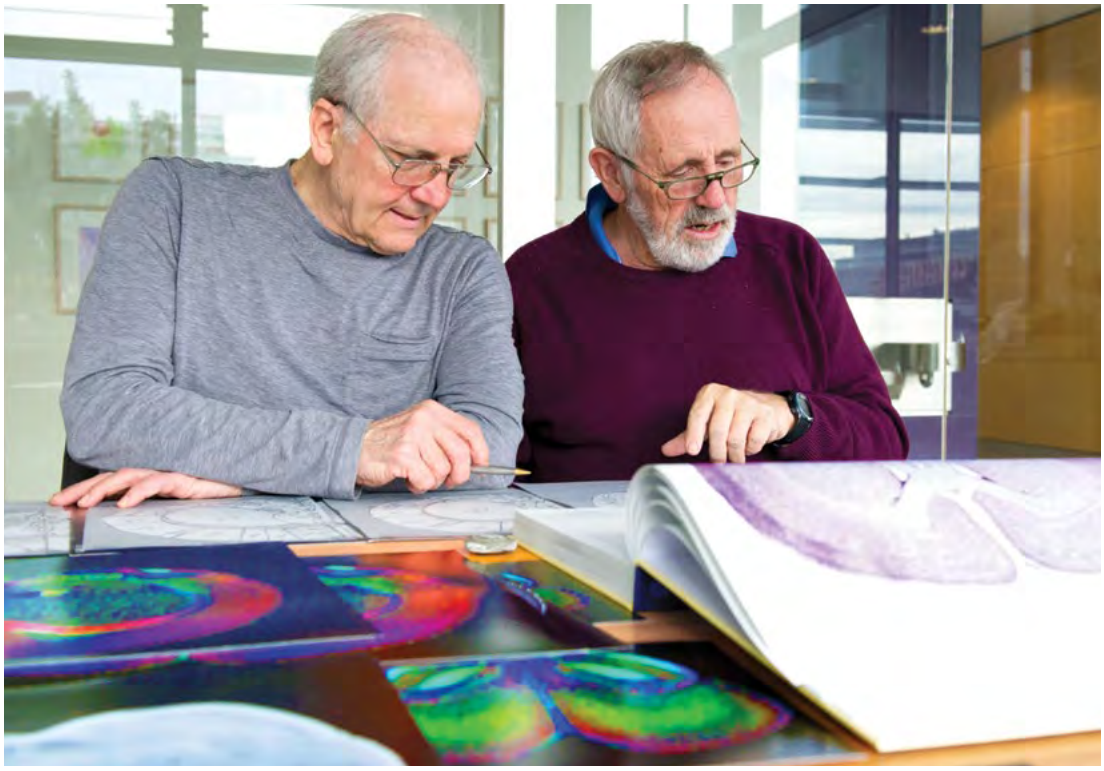
To combat the monotony, the team has included more than 2000 different exercises on the app. It is completely responsive to the individual's ability and schedule and can be used for 10 minutes or 40, depending on the person's time constraints.

Eighteen months in the making, the app was designed with guidance from medical literature, systematic reviews and feedback from focus groups of older people. Each exercise has an instructional video as well as visual and audio clues to guide participants along the way.

Over 2000 different exercises are included in the Standing Tall app

BRAIN MAPPING

Profs Paxinos and Watson have revisited their renowned work *The Rat Brain in Stereotaxic Coordinates* and recreated their anatomical maps of the rat brain in high resolution magnetic resonance and diffusion tensor images.



Profs Paxinos and Watson use cutting-edge images to produce a new generation of brain atlases

One of the most important tools in brain research, an atlas that maps out the various regions and pathways in the rat brain, has been updated thanks to the latest in medical technology.

The Rat Brain in Stereotaxic Coordinates, which was first published in 1982 and is now in it's seventh edition, is a staple for medical and neuroscience students as well as the most cited reference tool used by neuroscience researchers and clinicians.

Accurate brain atlases are essential to studies that use animal models of human brain pathology, such as in Parkinson's disease and Alzheimer's disease. Until now, rat brain atlases contained histological maps, which are images of thin sections of brain tissue taken at a microscopic level that have been stained, photographed and had various anatomical areas identified.

Recently, an expert in high resolution magnetic resonance imaging (MRI) at Duke University, USA produced the best magnetic resonance and diffusion tensor images currently available in the world. "These images offer greater detail and allow researchers to take advantage of new MRI technology, including the fact that the living brain can be scanned many times without causing injury," says Prof George Paxinos.

Profs Paxinos and Watson used these cutting-edge images to produce the first of a new generation of brain atlases that is directly compatible with their leading histological atlas.

Published in 2015, *The MRI DTI Atlas of the Rat Brain* will soon be made available in a digital format to further support the work of neuroscience researchers, clinicians and students.

Dr Kim Delbaere, Profs Stephen Lord and Jacqui Close: collaborating to reduce falls in the elderly

HIP FRACTURE

Falls resulting in hip fractures are a major contributor to the disability in older people and a public health problem so research groups are collaborating to address the issue.

One of the most serious consequences of a fall in an older person is a hip fracture. It's a devastating injury and for many results in pain and lasting disability which directly impacts on the ability to live independently. There are approximately 20,000 hip fractures in Australia every year. Falls result from interplay between impairments in physiological functions, ageing and environments. There are myriad contributing factors, including drugs affecting cognition, inactivity, disease processes such as Parkinson's and stroke, and syndromes such as dementia and delirium. Preventing falls and effectively managing fall related injury is a key research and health priority.

The Falls, Balance and Injury Research Centre brings together the complimentary research of three senior research groups at NeuRA led by Prof Stephen Lord, Prof Jacqueline Close and Dr Kim Delbaere. The aims are the accurate documentation of falls and fall injuries, identification of fall risk factors, development of feasible fall prevention strategies and effective management of people with a fall related injury.

Our falls and injury epidemiology research uses multiple health service databases to examine factors contributing to and outcomes from a hip fracture. This includes identification of variation in practice across hospitals including differences in time to surgery and mortality.

NeuRA is also home to the Australian and New Zealand Hip Fracture Registry. Information is collected from hospitals across the country on hip fracture care with a view to using data to drive change in practice and ultimately to improve outcomes for older people.

BALANCE & VISION

Patients with balance disorders will be able to take their rehabilitation home with them.

The vestibulo-ocular reflex (VOR) is the key way we maintain our vision during unpredictable and rapid head movements. Without it the world would appear to bounce every time we took a step or drove on a bumpy road. The vestibular organs, one located in each inner ear, sense the movement of our head and rotate the eyes to counter this movement so that our vision is kept stable.

When the vestibular organs are affected by age or disease, the result can cause feelings of vertigo or dizziness, but by far the biggest complaint is unstable vision during any activity that involves head movement. Assoc Prof Americo Migliaccio and his team have created a rehabilitation device that can be used to help 'train up' the VOR in people whose vestibular organs have been impacted by ageing, disease or injury.

The device is based on a training technique developed by NeuRA's Assoc Prof Migliaccio and Assoc Prof Schubert from Johns Hopkins University, USA. Their aim is to make sure it can be effectively used at home. Unlike previous methods, the technique is practical for vestibular rehabilitation and produces a significant increase in VOR response.

"We have achieved our first aim of building a rehabilitation device that can withstand the rigours of daily home use," says Assoc Prof Migliaccio. "Our current aim is to track VOR function, vision during head movement, standing balance, walking balance and quality of life in two randomised groups of patients with vestibular organ injuries over one week (our short-term clinical trial) and over one year (our long-term clinical trial)."

In one group, patients will use the rehabilitation device once daily for 15 minutes at home using the new training technique, while the other group will undergo the current best practise technique.

LEADERSHIP

BOARD OF DIRECTORS

NeuRA is established as an independent, not-for-profit company, Neuroscience Research Australia. Directors of the NeuRA Board and the NeuRA Foundation Board serve in an honorary capacity.

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The NeuRA Foundation is responsible for fundraising and communications activities.

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FOUNDATION

In 2008, Michelle was devastated when her father, Jack, passed away from Multiple System Atrophy (MSA), aged 83. Then, only two years later, Michelle was similarly diagnosed with this fatal neurodegenerative disease.

Michelle Baltins

Knowing that important MSA research is happening right here in Australia gives me hope for others in the future, albeit now too late for Michelle.

"At the time, Michelle and her father were the only recorded parent-child occurrence of MSA. Michelle was the eldest of three children and she idolised her parents. Before her diagnosis, she was a vivacious and successful sales executive whose passions included skiing, swimming, her golden retriever and travel. She had glamourous movie-star looks and her vibrant personality meant she was always noticed and rarely forgotten. She had a great sense of humour and she continued to share a special bond with her step-grandchildren, even after her ability to speak was taken.

Michelle passed away in 2015. Prior to her passing, we had decided that asking loved ones to make a donation to MSA research at NeuRA in her memory was really important. Michelle strongly supported research. While she was still able to, we travelled the world meeting with leading scientists and clinicians.

When the time came, we chose to support NeuRA. They had received the first NHMRC funded research grant into MSA in Australia and they continue to collaborate with MSA researchers around the world to find what causes MSA.

Knowing that important MSA research is happening right here in Australia gives me hope for others in the future, albeit now too late for Michelle."

Edgar Baltins: Giving in Memory

> *It was neither divine intervention nor lady luck that saved my life. It was a combination of knowledge, skill and the training of a special group of people.*

Evan ran the Half Marathon raising funds for NeuRA

Evan took part in the SMH Half Marathon as a 'NeuRA Runner' raising awareness and funds for NeuRA.

"In 1999 I experienced a major rupture in the left side of my brain. I was pretty much a goner. Fast forward to today and the only evidence of my aneurysm is a partial paralysis of my right foot, knee and hip and some pretty epic scars on my head. Mum calls it a miracle; others say I was lucky to survive. I know better. It was neither divine intervention nor lady luck that saved my life. It was a combination of knowledge, skill and the training of a special group of people who dedicate their lives in an endless pursuit to prevent, cure and treat brain injuries and disorders."

Evan: Fundraiser

Ruth and Jacqui, mother and daughter, participated in the NeuRA Memory Cycle to Vietnam and Cambodia raising funds for Alzheimer's research.


Ruth and Jacqui Dosser

"It was a trip of a lifetime! We both travel extensively but this trip was completely different, something you can't get anywhere else. We met inspiring people who we are still in touch with and we are going to do another trip together again in support of NeuRA. This holiday brought us closer and it was the best way to bring people together and support a cause very dear to our hearts. Until you do a trip like this you can't possibly know how it will transform your life and the lives of so many others. It's a beautiful rewarding thing. We can't wait to meet more amazing people and catch up with our new friends on the next trip."

Ruth & Jacqui Dosser: Fundraising

> *Meeting like-minded people who want to not only challenge themselves but also transform their holiday into an adventure that will make a difference in this world is truly special and unique.*

“World health demands continuing scientific research and NeuRA is actively meeting this challenge.”


Betty C Lynch OAM

Betty Lynch is supporting research into bipolar disorder as her late husband John suffered with the disorder.

“After searching for years for answers, I found Prof Peter Schofield’s research into bipolar hence my introduction to NeuRA. World health demands continuing scientific research and NeuRA is actively meeting this challenge. Supporting The John and Betty Lynch Seminar Room will promote intimate discussion, and exchange of ideas with NeuRA researchers and visiting professionals. This year I am also supporting two scientists in gaining international experience with leaders in bipolar research. It is a great privilege to be given this opportunity.”

Betty C Lynch OAM: Major Donor


Maria and Jeanne on the set of The Mike Walsh Show when they sang with the Geoff Harvey Orchestra

Maria Venuti, Jeanne Little’s close friend, celebrated by supporting The Jeanne Little Alzheimer’s Research Fund.

“It is so difficult seeing my vibrant, beautiful friend, with a heart of gold, not even recognising me. Every time I see her I pray that I might see a sparkle, a glimpse of my dear ‘bosom buddy’. I feel blessed to have this major celebration of my 75th birthday, surrounded by my family and friends and so it just felt right to mark this occasion with a huge party that would also raise funds for The Jeanne Little Alzheimer’s Research Fund at NeuRA.”

Maria Venuti: Giving in Celebration

Doug Mitchell joined our bequest program, *Commitment to Cure Society*, to honour his late wife Bobbi who had Alzheimer's. He has also decided to participate in our brain donor program.

"I felt that other areas of research get a lot of publicity. Neuroscience research is underfunded and no-one seems to be worried about it! It's so important to show our financial support, particularly for the future, and especially for Alzheimer's. It's simple really, this research has to be well-funded. It's essential."

Doug Mitchell: Bequestor

Doug Mitchell

Anthony signed up to NeuRA's *See it Through to A Cure* regular giving after reading about NeuRA's motor neurone disease (MND) research.

Anthony's parents, Bill & Norma, on their wedding day

"My father, Bill, died at 59 from MND and my grandfather at 65. This disease has now taken many members of my father's family. I'm now approaching the age when my father was diagnosed, and with my mother Norma in the late stages of dementia, I am keen to increase my giving to medical research and to making a difference. As an archaeologist, I know the important lessons we can learn from our pasts and how each little piece contributes to a bigger picture. In much the same way, I appreciate that the research at NeuRA contributes to the overall understanding of MND and diseases of the brain and nervous system and that by making a regular gift I am helping to make that difference."

Anthony Lowe: Regular Giver

"I'm now approaching the age when my father was diagnosed, and with my mother in the late stages of dementia, I am keen to increase my giving to medical research and to making a difference."

SCIENCE IN THE MEDIA

Dr James McAuley offered expert commentary on the benefits and drawbacks of the placebo

Science communication is more than simply sharing the latest research happening at NeuRA. It's an opportunity to encourage fellow scientists, inspire supporters and offer hope to those affected by a disease or disorder.

"Communicating science through the media plays an important role in bridging the gap between the scientist and a community seeking the latest research discoveries."

The media have been keen to access the expertise of our researchers across a whole range of topics. Prof Peter Schofield spoke with ABC News about an international study to which he and Dr Jan Fullerton contributed. It investigated how a patient's genetic make-up could impact the effects of the drug lithium, which is used to treat mood disorders including bipolar and depression.

Dr Muireann Irish was awarded the L'Oreal UNESCO For Women in Science Australia and New Zealand Fellowship, which caught the attention of *Vogue Australia* and *The Daily Telegraph*. Both publications wrote about Dr Irish's research into dementia, and also shared her passion for encouraging more young women to enter and remain in the field of science.

Science shows on television are equally keen to speak with NeuRA scientists. Dr James McAuley offered expert commentary, as well as some personal stories, during the SBS program *Insight*, which looked at the benefits and drawbacks of the placebo. While Prof Lorimer Moseley spoke in-depth to ABC's *Catalyst* program about his research, which is transforming our understanding of chronic back pain and opening the door to new treatments.

Importantly, researchers like Prof Simon Gandevia are able to take a broader look at science and start some important national conversations. Prof Gandevia spoke with Robyn Williams on Radio National's *The Science Show* about the cognitive errors and biases that many scientists fall prey to, and how these can be avoided.

Communicating our science through the media continues to play an important role in bridging the gap between the scientist and a community seeking the latest research discoveries.

NEURA'S DIGITAL VOICE

Through our digital channels, NeuRA continues to give voice to the innovative research emanating from our laboratories.

Triggered by a universal shift in communication technologies, there is a need for our scientists to explore new opportunities for public engagement through an increased stake in the digital environment. This ensures a wider impact for our research outcomes and promotes a two-way conversation.

From highlighting studies on schizophrenia to improvements in child safety in cars, the DIAN study, preventing falls in the elderly, or emotional development in teenage boys, we have increased our stake in internet-based "new media".

Our Facebook posts raise some interesting questions from people looking to know more about our findings or wanting to participate. Carers now have a forum to support one another, not only via our YouTube channel that allows seminars to be listened to at home, but also from the NeuRA Frontier's Facebook page. Our @motorimpairment twitter feed disseminates research findings and engages with leading scientists and journals from around the world.

NeuRA's blog highlights new work from our scientists and continues to gain readers worldwide. The Motor Impairment blog highlights not only our research in this field but implications on findings and future directions. The blog also provides an opportunity for research participants and supporters to tell their own stories about their partnership with NeuRA.

This is a two-way conversation, no more so than with the work of our Foundation. From fundraising events to treks in China, people have signed up and donated online, asked questions and encouraged us.

We have a vibrant online community and invite you to log in and discover more about what we do.

MEDIA MATTERS

Following is a snapshot of recent media coverage

DR KRISTIN LAURENS: Radio National's *Health Report* explored children who hear voices.

ASSOC PROF OLIVIER PIGUET: *ABC radio* about the feeling we get that each year seems to flash by faster and faster.

DR BILL BROOKS: ABC Radio National's *All In The Mind* covered the latest in dementia research.

DR PENELOPE MCNULTY: *Channel 9* featured Wii-based rehabilitation therapy after having a stroke.

PROF ROB HERBERT: *Sydney Morning Herald* wrote about the benefits of stretching after exercise.

DR LIZ DE ROME: *Motorbike Writer* covered research on motorcycle safety gear.

DR JULIE BROWN: *Reuter's Health* published an interview for a study on seat belt safety.

DR KIM DELBAERE: *Australian Ageing Agenda* shared news of the new iPad program for preventing falls.

DR LEE WALSH: ABC Radio National's *All in the Mind* interviewed Lee for a Sense of Self story.

DR REBEKAH AHMED: *AlzForum* shared insights gained from a study on eating disorders in frontotemporal dementia.

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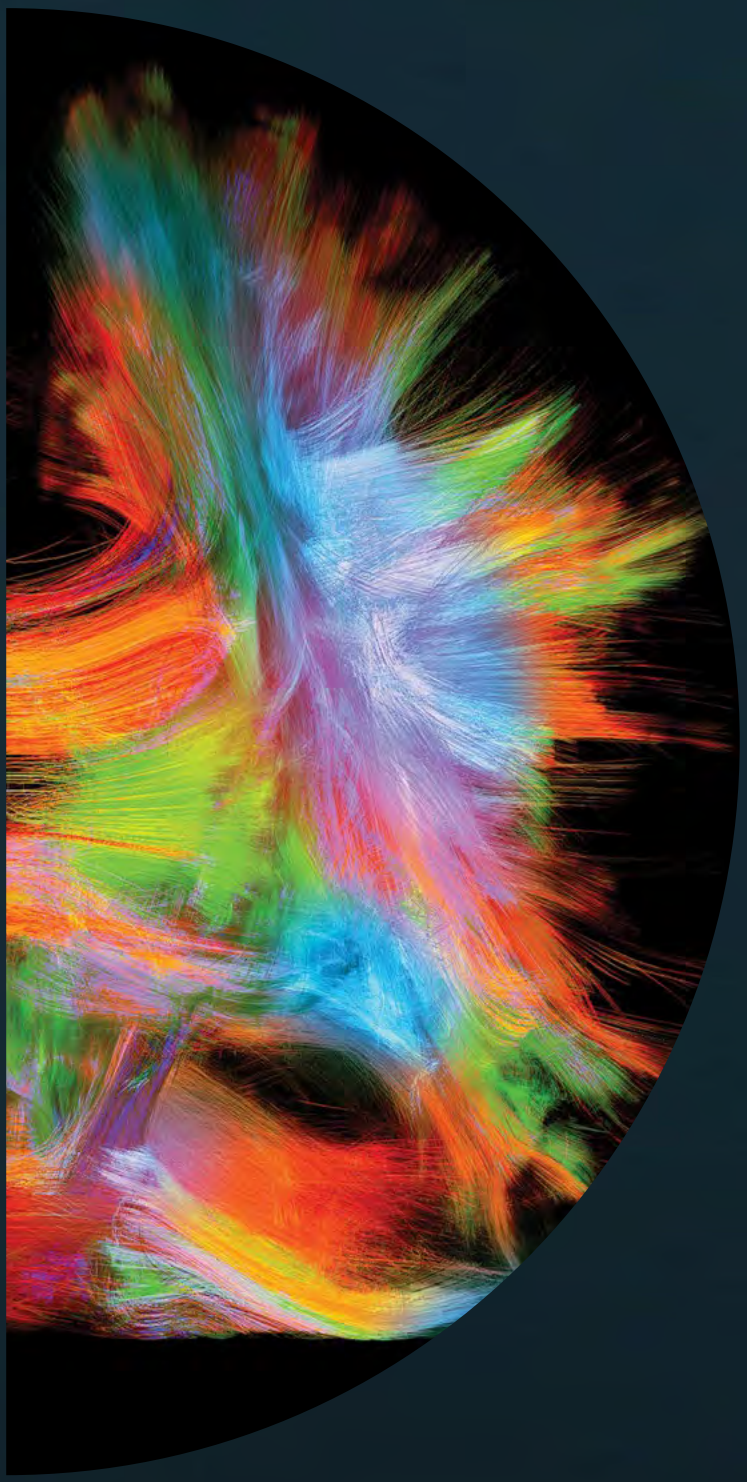

Editors: Chelsea Hunter, Anne Graham
Photography: Anne Graham
Design & Production: Designer Rice